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AMYOTROPHIC LATERAL SCLEROSIS.

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Writing on amyotrophic lateral sclerosis in The American Journal of the Medical Sciences in June, 1896, I said: "The clinical picture which is called up by this name is a well-defined one, and not subject to remarkable variation. So much cannot be said for the pathological process upon which the disease is dependent, nor for the morbid anatomical conditions found at the termination of the disease." The truth of this statement is substantiated by the case which I herewith record. That it is no uncommon experience for the post-mortem investigation of a case to show that the disease clinically typical is not dependent upon the classical lesion, viz., degeneration of both motor neurons, constituting atrophy and disappearance of the anterior horn cells and degeneration of the pyramidal tracts, is abundantly verified by the reports of cases cited in my first paper.

Amyotrophic lateral sclerosis is a rare disease, among the rarest of all organic nervous diseases. In my clinic the diagnosis has been made only six times in five years, during which period about seven thousand new cases of nervous diseases have come under my observation. In view of the fact that recent investigations have shown that some cases reported clinically as typical examples of this disease have been found to be dependent upon syringomyelia, myelitis, and internal hydrocephalus, it is not unlikely that in some of these cases the diagnosis was erroneous. To show further the rarity of the disease in ten years at the City Hospital, where chronic nervous diseases are very common, I have not seen upward of six or seven cases. The disease has been known to physicians for more than a quarter of a century. Char-

cot and Joffroy first described it in 1869, but general knowledge of the disease dates from Charcot's classical description in 1874. Still very little is known of its natural history, and absolutely nothing of its etiology.

Before entering upon some discussion of the nature of the disease and its occurrence, I present the history of a case with clinical and anatomical details, which throws some light upon one or more of the questions concerning the evolution of this disease which are yet unsettled.

Clinical Summary. Woman, aged thirty-six years. First symptoms, pain in neck and head, weakness of the upper extremities and of the muscles that support the head; atrophy and fibrillary twitchings of the muscles of the shoulder girdle, neck, and hands; profound exaggeration of all the tendon jerks; muscular hypertonia; slight spasticity of the lower extremities, and slight contracture of the arms and hands; Babinski phenomenon; no trophic, sensory, or sphincter disturbances; early and profound bulbar manifestations; duration of the disease about three years.—The patient, a married woman, aged thirty-six years, accustomed to housework, came under my observation June 17, 1897. Her family history was not of interest save that her mother died of tuberculosis. No history of nervous disease could be elicited. She had never borne children; her sterility had been attributed to uterine disorder, for which she had received much treatment, five curettements, and one laparotomy. The major operation was in 1892, and one curettage a year since then. When she came to the clinic in June, 1897, she complained of severe frontal headache and pain in the back of the neck radiating to the top of the head; of a tired feeling of the neck and shoulders; of inability to bend the neck forward when sitting with the head leaning back against a rest, and to lift it from the pillow when lying, without the aid of the hands; of profound "nervousness," especially when excited or annoyed; of tremulousness and weakness of the hands, at times of the entire body, and of weariness. A journey like that to the clinic makes her very tired; light housework fatigues her, shopping makes her nervous, depressed, and prostrated; putting up the hair exhausts her.

She cannot fix the time exactly when these symptoms came on, for she has not been in good health for seven years. She is positive that the nervous symptoms have developed within the past two years. In this time she has lost weight steadily, thirty pounds altogether.

Examination at this time showed well-marked atrophy of the right supraspinatus muscle and slight atrophy of all the muscles of the right shoulder, and of the right hypothenar eminence. All of these muscles are the seat of fibrillary twitchings, and their mechanical irritability is much increased. Their response to electrical currents is very sluggish, especially that of the right supraspinatus. The change is a quantitative one, there being no real reaction of degeneration. Inability to use the right upper extremity is proportionate to the atrophy. It was noted that she carried the head peculiarly: in a fixed position, thrown slightly backward, the chin tilted upward. This, taken in connection with the difficulty she has in raising the head when lying, bespeaks involvement of the trapezii muscles. The grip of the right hand is weaker than the left. Both hands seem to have lost their dexterity. The knee-jerks are lively, the right more than the left, both pathologically increased. There is

distinct ankle clonus on the right side, partial on the left side. The gait is not impaired, and she maintains that aside from weakness she walks as well as usual.

Sensibility unimpaired. The functions of the bowels and bladder are undisturbed. Deep pressure does not cause pain, although the atrophying muscles feel sore. The visual fields are normal, and there is no disorder of the special senses. The patient's voice is high-pitched, not modulated, and articulation is slightly impaired. Her features have a set expression, as if the emotional muscles were on the point of acting. (Fig. 1.)

FIG. 1.

Illustrating the "spastic" condition of the emotional muscles.

In the autumn of the same year, six months after the above history was taken, it was noted that the patient complained of dyspnœa, dysarthria, palpitation, easily induced fatigue, dysmenorrhœa, profound nervousness, lack of will power, mental depression, suicidal impulses, increasing helplessness, and of difficulty in swallowing. If food gets on the back of the tongue it must be dislodged with the finger; if she gets it out into the anterior part of the mouth and then shoots the tongue back quickly the bolus goes down. This is exhausting. The face gets tired on chewing and talking. There is occasional regurgitation through the nose. The atrophy of the right shoulder girdle has increased, and extended so that now all of the muscles, including the trapezii, are involved. (Fig. 2.) The hypothenar eminence and other muscles of the hand are not more conspicuously atrophied than before. Fibrillary twitching of the muscles, not only of the atrophied muscles, but of

others of the upper extremity that look normal, is very distressing. Myotatic irritability of all the muscles is very much increased, the knee-, ankle-, elbow-, and jaw-jerks being abrupt and exaggerated. The Babinski reflex is present. The gait is spastic, the stride slight, the strength feeble. The trunk is held rigid, the head fixed and tilted backward. The tongue is the seat of fibrillary tremor, and has the characteristic "bunched" appearance of atrophy. It can be protruded

FIG. 2.

Showing extreme atrophy of shoulders.

just beyond the lips. Intrabuccal motility is now much impaired. The lips have lost their alertness and can no longer be puckered. There is drooling at night. Vocalization and articulation are typical of bulbar paralysis. Attacks of dyspnœa, which are not infrequent, are most distressing to the bystander and agonizing to the patient.

The atrophy which the patient presented at this time is well shown by the accompanying photographs.

About this time she began to have profound hysterical attacks. The atrophy was now increasing rapidly. She had difficulty in maintaining the poise of the head. It tended when unsupported to fall backward or forward. (Fig. 3.) When the occiput approximated the nuchal region she could get the head forward by pushing it with the hands or giving a quick jerking motion forward, which set it up as if it were on a loose hinge. The atrophy of the muscles of the shoulder girdle on both sides was now so advanced that the heads of the humeri dropped from the sockets of the scapulæ, and there was proportionate limitation of movement.

FIG. 3.

Showing position of head when unsupported.

In the spring of 1899 she could still walk with short stride and slow step from one room to another with assistance. Spasticity of the lower extremities now first became considerable. During the entire course of the disease it was never prominent in the lower extremities, but now there was considerable resistance to passive movements, although the upper extremities had become quite powerless, but the bulbar symptoms predominated. The lips were decidedly atrophic. The tongue, which was before irregular and lumpy in its appearance, has become thin and ribbon-like, the seat of incessant vermicular movement. The soft palate, which cannot be raised voluntarily, is scarcely elevated on efforts of intonation, and swallowing is accomplished slowly and with great difficulty. Semisolids are taken most easily. They must be placed on the back of the tongue, then she swallows with great deliberation. Fluids

are regurgitated through the nose sometimes, and attacks of coughing, incidental to some of the food getting into the trachea, are not uncommon. The tendon jerks were all enormously exaggerated, the slightest tap on the patellar tendon sufficed to throw the foot up sharply. The ankle-, elbow-, and jaw-jerks are likewise very much exaggerated. The Babinski reflex was distinctly to be obtained. There were still no sensory, sphincter, or trophic disturbances. Mentally the patient was very much as before, depressed, despairing, and dejected. Threats of suicide were constantly being made. Her reasoning powers were, however, undiminished.

Her emotional state had attracted attention from the beginning. She had no hope, except at rare intervals. Despite her despondency and threats of self-destruction, she was quite sound mentally. The attacks which she began to have about a year before death, and which I have called hysterical, were ushered in with palpitation, tachycardia, and dyspnœa, followed by screaming and violence, as if an expression of agony; stiffness, opisthotonos, unconsciousness, which graduated into sleep, out of which she awakened limp and exhausted. Such an attack would last several hours if not cut short by chloroform inhalation.

A description of one of these attacks, taken from the notes of her case, is as follows: "She becomes frightened, anxious, fearful, tremulous, complains of a feeling of suffocation and of great weight on the chest, and clamors for air. She moans, cries out, thrashes about, and gasps for breath, the respiratory acts being very rapid and labored. Some of the movements that she makes in these attacks are astonishing; for instance, she was lying flat, and with what seemed to be one supreme effort she raised her head and body and bent forward until her forehead struck the bed at her knees, and then she went back again, like the rebound of a ball, to the pillow. She had been unable to raise her head without the assistance of the hands for some time. The pulse in these attacks becomes so weak and feeble that it is scarcely countable. She is sleepless, restless, cast down, wants to die, but is continually clamoring to get well, and cannot be reassured.

The patient died May 25, 1899, after a paroxysm similar to that above described.

The autopsy was performed about four hours after death. Great difficulty was encountered in obtaining a post-mortem examination, and only the brain and spinal cord were examined. The autopsy notes are as follows:

The hair of the scalp is coarse and extremely sparse. The pupils are equal and dilated. The tongue is small, thin, and pale. The skin is smooth, and there were no abrasions. The weight of the entire body is forty-eight pounds. There is extreme atrophy of the muscles of the hands, forearms, and upper arms, and complete atrophy of the shoulder girdles. Some rigidity of the lower extremities. The muscles of the back and of the legs are very small but firm.

The brain was easily removed. It was of average size, and, aside from slightly increased consistency, it was normal macroscopically. The meninges were anæmic and apparently normal. The spinal cord to the naked eye presented a normal appearance aside from the increased consistency in the fourth cervical segment, to be described later.

The cord was carefully segmented, and each segment divided into three pieces for alcohol, Marchi and Müller hardening. Thus prepa-

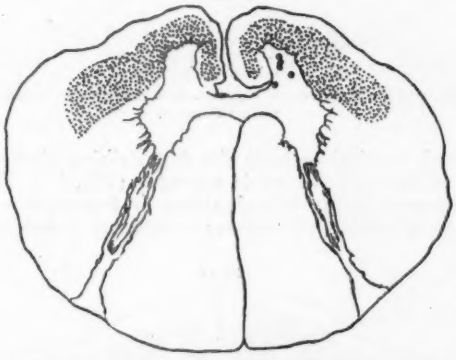
rations of Nissl, Marchi, Weigert, and picric acid fuchsin were obtained from each segment. Of the lower portion of the cord alternate segments were placed in various fixation fluids.

The oblongata was hardened in formaldehyde alcohol, and the brain in Lang's fluids. I am indebted to Dr. Carlin Philips, instructor of neurology in my clinic, for preparing the specimens—a very considerable task, painstakingly done.

In describing the histopathological changes I shall present briefly the picture of a few of the segments in series.

Second cervical segment, Weigert stain: The neuraxons constituting the columns are normal, with the exception of two symmetrical degenerated areas, as follows: A concentric zone encircling each anterior horn, beginning at the base of the anterior median fissure between the direct pyramidal tracts and the mesial border of the anterior horn, thence encircling the apex of the horn and extending nearly to the peripheral margin of the cord. (Fig. 4.) Thus the tracts involved in

FIG. 4.



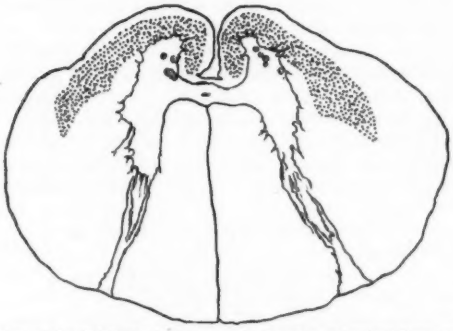
Second cervical segment, showing the extent of degeneration in the white substance.

the degeneration are the antero-mesial and antero-lateral of the fundamental columns. Gowers' column, the direct pyramidal tract, and a thin marginal zone skirting the ventral periphery of the cord, are left intact. Although the degeneration spares the ventral marginal zone and the columns of Gowers, it is nevertheless possible that some neuraxons in both tracts may be involved. Scattered through the entire anterior and antero-lateral fundamental columns are many fibres which are normal in every respect. In sections stained with picric acid fuchsin one sees that the neuroglia proliferation is but slight in the areas that show such distinct degeneration with Weigert's stain. In one anterior cornua the motor cells, with the exception of two, have entirely disappeared, while on the other six are to be seen. The smaller cells of the lateral horn appear normal in number and structure.

In the third cervical segment the cornet-shaped area of degeneration is seen to extend dorsally to a greater extent in the lateral columns. (Fig. 5.) The absence of the motor cells is striking, the average number being about two in one anterior horn and four in the other. This

great loss of anterior horn cells, from the upper portion of the second cervical to the lower portion of the third cervical, probably amounts to 90 per cent., and corresponds very well to the loss of function of the deep muscles of the neck. The small elongated cells of the intermediate zone appear to be normal in every way.

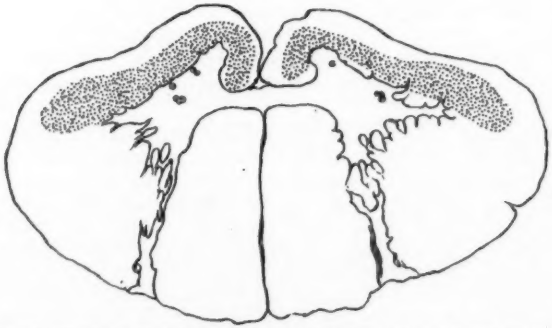
FIG. 5.



Outline drawing of the third cervical segment, showing extent of degeneration in the white substance.

In the fourth cervical segment the first striking change in contour and volume of the cord as a whole appears. (Fig. 6.) The deformity in outline is present in the following four or five segments below. It consists of an alteration of contour caused by a sinking in of the

FIG. 6.



Fifth cervical segment, showing change in the contour and volume of the cord, scarcity of cells in the anterior horns (the cells are represented by circles), and degeneration in the white substance. (Composite drawing. Weigert stain for degeneration, carmine for the cells.)

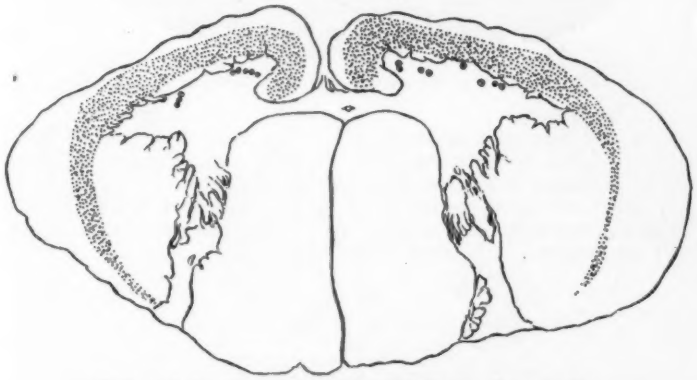
periphery at the point of emergence of the anterior roots. In fact, the periphery of the cord from a point corresponding to the apex of the anterior horn to the lateral tip assumes a concave instead of a convex line. Obviously the retraction of the ventro-lateral periphery of

the cord on either side of the anterior median fissure is due to the contraction of neuroglia growing in the degenerated area described. Inasmuch as this deformity of the cord's contour is not present in the second and third cervical segments, we may assume that the neuroglia in these t › segments is of more recent origin than that in the fourth segment.

The area of the degeneration shows some further variation from the previous segments on account of change of shape of the ventral horns of gray matter, the gray matter of the fourth cervical segments extending laterally so as to thrust the lateral horn toward the periphery. The degenerated area from here on thus assumes a sickle shape. (Fig. 7.)

Another respect in which this segment differs from those above is in the degeneration of the marginal zone just ventral to the mesial and lateral boundary of the anterior horn. Aside from these degenerative changes in certain areas as described, the remainder of the white substance appears to be normal.

FIG. 7.



Sixth cervical segment, showing sickle-shaped area of degeneration.

Sections from this level stained by the Nissl method show only three or four large motor cells in each ventral horn. This is an extraordinary decrease in the number of cells, as in the normal cord one can count fifteen to twenty-five. The number of medium-sized and small cells in the region of the gray commissure is not so greatly reduced. In contrast to the findings in other levels of the cord, the lateral horn group at this level is entirely absent. As regards the histological process which caused the disappearance of these cells, the serial phases of it are difficult to formulate, for the reason that the cells that are present are fairly normal. While it is obvious that thousands of cells have disappeared, it is nevertheless difficult to find a single cell body which is actually going to pieces or which shows unmistakable evidences of disintegration. The question is, "How do they disappear?" We find no particular evidence of their destruction, and yet with even a low-power inspection the most striking feature of the whole case is the absence of these cells without a trace of their existence. The remaining cells usually show some confluence of chromophilic plaques into a homo-

geneous mass and yellowish pigment granules which are crowded off into one pole or extremity of the cell. But between this condition of the cell and its ultimate disappearance no intermediate phases can be found.

A brief summary of the findings in Nissl preparations may be made as follows:

FIG. 9.

Weigert stain of the eighth cervical segment, showing deformity of the anterior horns.

1. A fair proportion of the anterior horn cells that have escaped destruction show no great departure from the normal except fogginess and indistinctness of outline of the chromatic plaques.

2. Other cells show confluence of plaques and have masses of yellowish pigment in the protoplasm. The cells of this second class apparently are atrophic. These are illustrated in Fig. 8.

FIG. 10.

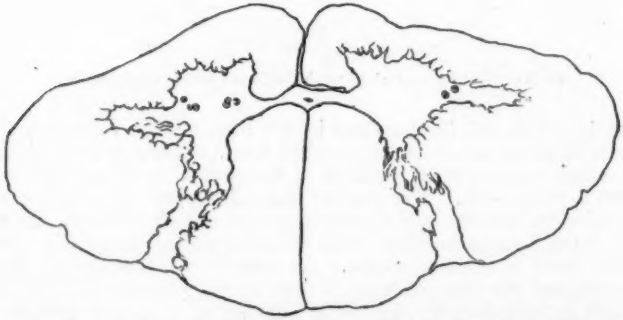
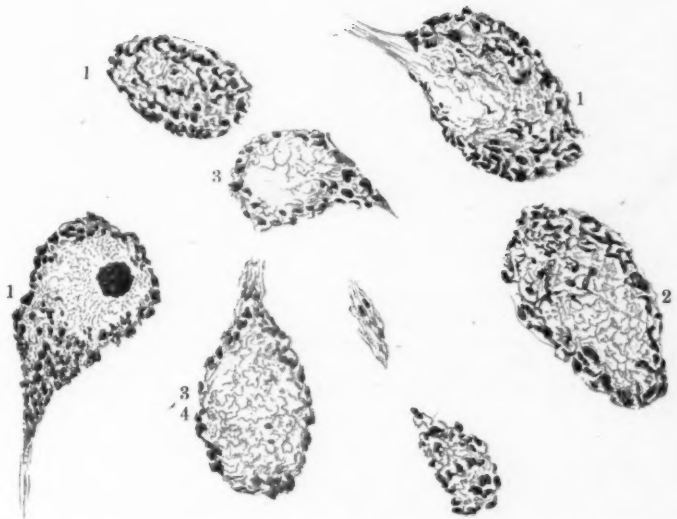


Diagram of the seventh cervical segment, to show paucity of cells in the anterior horns.

Fifth cervical segment practically the same as the fourth cervical.

Sixth cervical segment. In this segment the degeneration extends dorsally in a symmetrical way, forming a tongue-shaped area between the crossed pyramidal and the direct cerebellar tracts, reaching to the end of the posterior horn. The anterior horns are more flattened than in their normal condition, and lie nearer to the ventral periphery

FIG. 8.

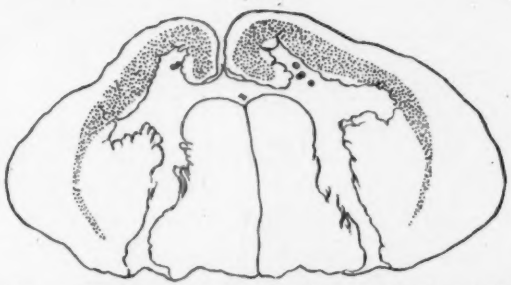


Cells of the anterior horns, showing indistinctness of outline (1, 1, 1) of chromatic plaques; masses of yellow pigment (2); plasmolysis (3, 3); chromatolysis (4).

of the cord. The large motor cells of this segment as seen in Nissl preparations show some diminution in number, corresponding proportionately to those observed in the preceding segment; also, the lateral horn group of cells has disappeared.

In the seventh and eighth cervical segments the area of degeneration of white fibres has the same relative distribution, except that it reaches

FIG. 11.



To show the area of degeneration in the white matter at the eighth cervical segment.

further inward toward the lateral horn. The anterior roots show marked degeneration when examined by Weigert's method. (Fig. 9.) The cells of the anterior horn are very few (Fig. 10), and are degenerated as well as the groups of cells in the lateral horns. (Fig. 11.) The direct cerebellar tract in this segment shows a few degenerated fibres.

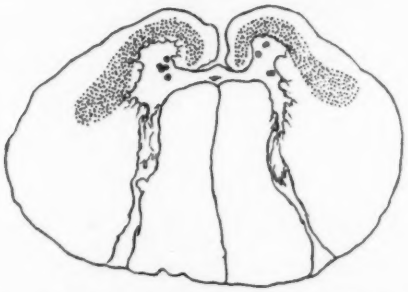
FIG. 12.

First dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the level of the first dorsal to the fourth, inclusive, the type of fibre degeneration takes the form shown in the upper cervical region, namely, a zone encircling the anterior horns, becoming progressively smaller and less and less intense, until at the level of the fourth dorsal it is scarcely discernible, except for a slight and ill-defined pallor encircling the apex of the ventral horns. (Figs. 12, 13, and 14.)

The disappearance of the motor cells is somewhat more difficult to determine throughout these first four dorsal segments than in the cervical segments, since normally there are so few cells in the ventral horns. There can be little doubt, however, that the atrophy of the cells is present in these segments in about the same proportion as in the cervical cord. The lateral horn cells and those of Clarke's column appear to be normal in these segments.

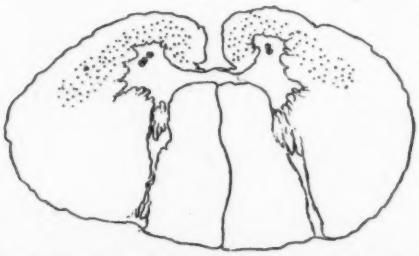
FIG. 13.



Second dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the fifth to the eleventh dorsal segments the degeneration of the fundamental columns is so slight that it is hardly apparent in sections stained by Weigert's method, yet in picric acid fuchsin specimens there is seen to be present an increase in neuroglia tissue. This confirms the idea that the same degeneration exists, but to a less extent, throughout the entire dorsal region.

FIG. 14.



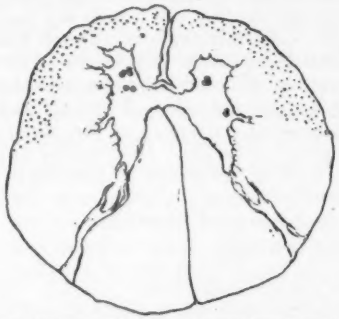
Third dorsal segment. Stippled area corresponds to the degeneration.

What has been said regarding the condition of the motor cells of the upper dorsal also applies to segments of the lower dorsal region. The cells of the lateral horn are normal, while here and there in Clarke's column are groups of cells which are atrophic and are pigmented, with excentric nuclei.

From the twelfth dorsal to the third sacral, inclusive, the zone of degeneration in the ventral half of the spinal cord assumes a radically

different position from that found in other regions. (Fig. 15.) It occupies the peripheral lamina of the ventral half of the cord extending from the lips of the anterior fissure around to a point opposite the apex of the lateral horn, where it expands to a triangular mass indenting deeply inward the region of the cord just ventral to the crossed pyram-

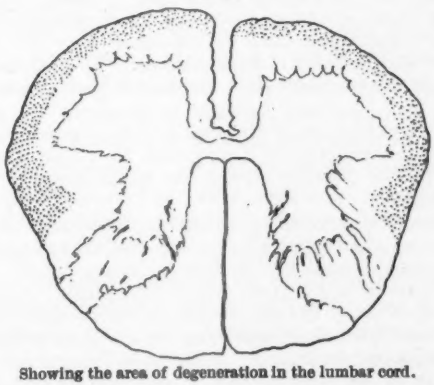
FIG. 15.



To show the degenerated area approaching the periphery.

idal tracts. It may be briefly described as a comma-shaped area, the head of the comma lying against the ventro-lateral border of the crossed pyramidal tracts, and the attenuated tail of the comma extending thence around the periphery of the cord nearly to the lips of the anterior median fissure. (Fig. 16.)

FIG. 16.



Showing the area of degeneration in the lumbar cord.

Relatively speaking, the anterior horn cells throughout the lumbar and sacral regions of the cord are as much diminished in number as in the cervical region. Because the lower extremities were active long after the involvement of the upper ones, we had expected that the lumbar and sacral regions of the cord would show a corresponding

immunity from disease of the anterior horn cells, but such is not the case. I was again disappointed in not finding stages of cell atrophy which would enable me to determine the actual process of dissolution of the cells. Here, as elsewhere in the cord, the cell is either fairly normal in appearance or it has completely disappeared. Throughout the cord the bloodvessels seen are normal.

In the medulla oblongata, from the sections taken at the lower one-fourth of the hypoglossal nucleus, one cannot say that there is any striking loss of the cells. Certainly there is no such loss in this nucleus to correspond with the striking loss of motor cells of the cord. There are, however, positive signs of structural changes, although these are limited to a small proportion of all the cells. Those affected show eccentricity of the nuclei, homogeneous conversion of the chromophilic plaques, or a filling up with pigment granules. I am unable to record any signs of cell disintegration, such as shrinkage or distortion of the cell body. These same anatomical findings are present in the nucleus ambiguus. From the scattered and isolated distribution of this nucleus it is quite impossible to say that degeneration of it exists in a given instance unless it is practically destroyed. Such is not the condition in this case.

The dorsal vagus nucleus is apparently normal. In Weigert preparation of the oblongata from this region the posterior longitudinal bundle is seen to be slightly but distinctly degenerated. This is what we might expect from its relation to the anterior and lateral ground bundle of the cord. Aside from these changes the oblongata was normal. The internal capsule and the corpus callosum were not examined.

Pieces of the motor cortex hardened in Lang's fluids were examined. The large motor cells from the paracentral lobule and from the Rolandic area show a pallor which at first seems to be indicative of structural change. It appears that this change is not confined to these cells, but affects uniformly all the cells of the cortex. These cells are quite as numerous as normal, so having used such an unsatisfactory reagent as Lang's mercuric hardening fluid we concluded that the change is an artefact rather than a true structural change. No statement can, therefore, be made as to the presence or absence of pathological changes in the brain.

The pathological findings of this case may be summarized as follows:

1. Uniform disappearance of the ventral horn cells throughout the entire cord, affecting (possibly) the dorsal region less severely than the cord enlargements.

2. Degeneration of a zone in the anterior fundamental columns skirting and encircling the ventral horns in the cervical and upper dorsal regions, also the anterior portion of the lateral limiting layers. (Bechterew.)

3. Degeneration of a marginal strip of the ventral periphery of the cord expanding dorsally against the ventral and lateral border of the crossed pyramidal tract, and appearing with a comma-shaped head in the lumbar and sacral regions.

4. Deformity of the ventral face of the cord in the cervical and upper dorsal region due to a concave sinking-in of the periphery.

5. Neuroglia proliferation in the degenerative area of white matter, and also in the anterior horns of the cord enlargements.

6. Evidence that the neuroglia proliferation is older in the cervical region. The degeneration is denser in the region and has caused shrinkage of the ventral face of the cord at the emergence of the roots.

7. Atrophy of the anterior roots.
8. Distinct evidence of cell degeneration (chromatolysis, plasmolysis, and disintegration) in the hypoglossal nucleus and the nucleus ambiguus.
9. The pyramidal tracts are intact.

Amyotrophic lateral sclerosis is a disease characterized by the symptoms of progressive muscular atrophy of the Aran-Duchenne type, complicated with bulbar involvement, plus spastic paresis, particularly of the lower extremities, and exaggeration of the tendon jerks all over the body. The morbid process upon which it is dependent consists in a decay of the peripheral motor neurons in the ventral horns, the terminal arborizations of the central motor neuron (in other words, the ending of the neuraxons that come down through the cord as pyramidal tracts), and of the pyramidal tracts themselves, and atrophy of the column (strange cordonal) and commissural cells of the gray matter. The degeneration extends centrifugally in the peripheral motor neurons, centrifugally and centripetally in the central motor neurons. This constitutes when the process is complete a characteristic microscopic picture, the principal features of which are (1) atrophy of the anterior horns and diminution or disappearance of all its cell constituents without noteworthy change in the bloodvessels; (2) degeneration of the fundamental tracts of greater or lesser extent; and (3) degeneration of the pyramidal tracts which may be so slight as to be scarcely detectable, or so complete that it may be traced to the origin of these tracts in the motor cortex. The question whether the peripheral motor neuron—*i. e.*, the root cells of the anterior horns, or the central motor neurons—the pyramidal tracts—are the first to be involved, cannot yet be answered.

Neurologists are well aware that there is much difference of opinion as to the starting-point of the disease. Charcot and the Parisian school generally, with the exception of Brissaud, maintain that the lesion is primarily and predominantly (at least in the beginning) of the central motor neurons, the pyramidal tracts in the spinal cord being diseased first, and that the affection of the white matter is consecutive or "deuteropathic." Brissaud's idea seems to be that the primary seat of the disease is in what Marie calls the supplementary zone, an area ventral to the pyramidal tracts and dorsal to the intermedullary anterior roots made up of the prolongations of column cells in the gray matter uniting different levels of the cord. The pyramidal fibres are involved later, and, finally, the ventral horn cells. This, however, presupposes the secondary involvement of the gray matter, which is the question in point. Dejerine and Thomas, commenting upon this view, say that this opinion of Brissaud is invalidated by the facts. The fact that the lesion of the motor cord is not strictly confined to the pyramidal tracts, but invades the antero-lateral, speaks in favor of Charcot's view. They then proceed to say that the degeneration of the pyramidal tract in

amyotrophic lateral sclerosis is for them indisputable, because they have always found it. This is a denial of the validity of the work of others as well as an expression of finality that few scientific men permit themselves.

Leyden was the first to contest this teaching of Charcot, and he has unswervingly maintained his position. His view is that the peripheral motor neuron is first and predominantly affected, and that the changes in the white matter are sequential. This view is shared, in a measure at least, by many of his countrymen. Gowers teaches practically a similar doctrine, namely, that amyotrophic lateral sclerosis is a variety of progressive muscular atrophy in which the pyramidal tracts are more profoundly affected than they are in the ordinary form of spinal progressive muscular atrophy. This is the view held by many neurologists in this country, for instance, Dana and Sachs.

As a matter of fact, it is impossible to say dogmatically, from histological study of our cases, whether the peripheral or the central neuron is affected first. The truth is probably that in one case the central neuron is diseased first, and in the other the peripheral. When the central neuron is affected first it is likely that the degenerative process begins in the central convolutions and not in the cord. This involvement of the cell body of the central motor neurons causes decay of the entire neuron, beginning in the most remote part—that is, in the spinal cord, the pyramidal tracts, the intercalary neurons, and the terminal ramifications around the anterior horn cells. The fact that the degeneration of the pyramidal tracts progresses upward does not speak against the primary cortical involvement; in fact, it speaks rather in favor of it.

It seems to me that we must admit, because of such a case as the one published herewith, that the lesion in some cases of amyotrophic lateral sclerosis begins in the cells of the anterior horn, and that destruction of the cells therein situated causes the phenomena (in part at least) of the disease, and accounts for the pathological findings. The cells of the anterior horns are of three distinct varieties. First, those which give rise to the anterior roots of the spinal nerve (root cells); second, those that send their prolongations from one side of the cord to the other (commissural cells); and, three, column (cordonal) cells—cells whose prolongations bind one segment of the cord to another by means of so-called association fibres. It is the degeneration of these column cells that causes the area of degeneration in the white matter of the cord in our case. Decay of other fibres, such, for instance, as the fibres of the column of Gowers, was probably incidental to the destruction of these short fibres. It is well known that column cells are to be distinguished from root cells not only by their histological peculiarities, but by their location. They are particularly numerous in the enlargements of the cord, and they occupy a region in the middle of the anterior horn close

to its junction with the posterior horn ventral to the column of Clarke, and to the column of cells described by Onuf and myself in the cat, which we called the paracentral column. The adjacency of these cells to the column of Clarke accounts for the existence of changes in the direct cerebellar tract in some cases which have been described, the lesion of the column cells implicating by contiguity some of the cells of Clarke's columns.

Destruction of these cordonal or column cells causes the degeneration of the fundamental columns in cases of amyotrophic lateral sclerosis and progressive muscular atrophy of the Aran-Duchenne type. That such degeneration does not occur in every case of either one of these diseases in no way invalidates what has been said. In the majority of cases of spinal progressive muscular atrophy such degeneration does not occur, and the explanation is that in such cases the destructive lesion in the spinal cord confines itself to the root cell (*i. e.*, to the ventral portion of the anterior horns), and that the column cells are not implicated. When they become implicated the supplementary zone in the gray matter is found diseased, as was the case in some observations of J. B. Charcot. It is not unlikely that this explanation suffices for all the cases of progressive muscular atrophy with changes in the white matter.

As to the explanation of the spasticity and exaggerated reflexes in a case like ours or that of Wolff, it must be sought for in some alteration to the central motor neuron in the brain which has not as yet extended to such a degree as to cause discernible alteration of its prolongation in the spinal cord.

What has been said should not be construed to mean that the lesion of amyotrophic lateral sclerosis is not often, perhaps always, if the disease lasts long enough, a degeneration of both systems of neurons throughout their entire course. That this is so there cannot be the shadow of a doubt. There are now eleven cases on record (the two cases of Kojewnoff, two of Charcot and Marie, one each of Lennmalm, Lumbroso, Nonne, Strümpell, Mott, Hoche, Spiller, Czyhlarz and Marburg) in which the pathological process involved both systems of neurons in their entirety. My contention is merely that such involvement is not necessary for the existence of the disease clinically. It may exist in its most typical form without any involvement of the pyramidal tracts whatsoever. This is shown by the cases of Wolff and Senator and by my own case. The case reported by Senator and by Wolff was clinically a fairly typical case of amyotrophic lateral sclerosis, especially in the latter stages. On microscopic examination of the specimens there were found atrophy of the anterior horn cells, arterial and venous hyperæmia, multiple punctate hemorrhages, apparently of recent origin, and incipient syringomyelia in the lumbar cord. The changes in the motor spinal cells explain the atrophy in this case, but there is no adequate

explanation of the spasticity. Dercum and Spiller, in commenting upon this case, inquire if they may not venture to suggest that the foci of softening around the hemorrhages had something to do with causing the spasticity. But Wolff has already considered this. In the first place, the softening was almost exclusively of the gray substance around the junction of the anterior and posterior horns, and of the posterior roots. That it could not have been due to the hemorrhages is shown by their recent occurrence. To explain the spasticity it may be fair to assume some involvement of the central motor neurons in the cortex which has not yet gone on to decay sufficient to produce degeneration at their termini. That spasticity may be caused by cerebral lesion without degeneration of the pyramidal tracts is well known. It occurs sometimes with hydrocephalus and with brain tumor, such as in a case diagnosticated as lateral sclerosis, recorded by Schultz, in which the autopsy showed only internal hydrocephalus. There was no trace of spinal-cord degeneration.

When the disease process of amyotrophic lateral sclerosis has reached its completion there can be no doubt, I think, that both motor neurons and the nerve elements which unite the motor nuclei of different levels together are involved, and this constitutes the typical lesion of the disease. Our case may be looked upon as one which stands midway between the cases in which the pyramidal tracts are pronouncedly affected and the case reported by Wolff. For a long time it was doubted that primary sclerosis existed as a pathological entity, although it had long been recognized clinically. The cases of Minkowski (*Deutsches Archiv f. klinische Medicin*, vol. xxxiv. p. 24) and of Dejerine and Sottas came near to fulfilling the requirements, but it was not until Strümpell, Donaggio (*Rivista Sperimentale di Freniatria*, 1897, vol. xxxiii.), and Kuhn (*Deutsche Zeitschrift f. Nervenheilkunde*, vol. xxxii. p. 144) published their cases that there was full substantiation of the existence of this condition. Primary lateral sclerosis must be a very rare disease, but not many years since the diagnosis of lateral sclerosis was not an uncommon one. Now it is rarely made. Careful following up of the cases in which such diagnosis was made has shown that they prove to be examples either of amyotrophic lateral sclerosis or multiple sclerosis; more the former than the latter. Moreover, since the establishment by Erb of the disease known as syphilitic spinal paralysis, some of the cases formerly diagnosticated as lateral sclerosis have found their proper classification there.

The changes in the spinal cord in amyotrophic lateral sclerosis are by no means confined to the anterior horns and the pyramidal tracts. The posterior columns, especially the columns of Goll, have been found diseased a number of times. For instance, the cases reported by Oppenheim, Charcot and Marie, Hektoen, Brissaud, Dercum and Spiller,

Luce, Dejerine, and Sottas. What the significance of these degenerations in the posterior columns is it is not possible to say. It may be that tabes has been superimposed upon amyotrophic lateral sclerosis, or *vice versa*, such as in a case of progressive muscular atrophy plus tabes about to be reported by me. It may be that the neuroglia overgrowth in the cord chokes off some of the fibres making up the columns of Goll, or it may be, as Marie suggests, that the cells of the gray matter that send their axis-cylinders into the posterior columns may be diseased, and thus cause decay of their prolongations.

The direct cerebellar tracts have occasionally also been found implicated by the morbid process. Stadelman was one of the first to call attention to the fact that degeneration of the lateral columns extends in some instances far beyond the confines of the pyramidal tracts, and this has been corroborated by many other observers, particularly by Marie, by Raymond and Ricklin, Spiller, Schlesinger, and others. Oppenheim gave what is probably the correct interpretation of this degeneration of the supplementary zone—*i. e.*, that it is due mainly to atrophy of short fibres uniting segments of the cord to one another.

That amyotrophic lateral sclerosis is a different disease from progressive muscular atrophy of the Aran-Duchenne type must be admitted, I think, also because of its very different clinical delineation. It is difficult to conceive of two diseases whose clinical course is more unlike. Progressive muscular atrophy of the Aran-Duchenne type is slow in its course, oftentimes lasting from five to fifteen years. Amyotrophic lateral sclerosis rarely lasts more than from two to three years. Of course, there are cases, such as that of Dejerine and Thomas, which last much longer, but these are exceptional. A patient with muscular atrophy does not seem to be ill for a long time after the onset of the disease, while in amyotrophic lateral sclerosis he is ill from the very beginning. In the latter there are no periods of cessation of progress or remission, such as there is not infrequently in spinal progressive muscular atrophy. And, finally, the different specific clinical features which differentiate the two conditions need not be here enumerated, as they are too well known. But that the two conditions cannot always be differentiated is well shown by an experience of Raymond. The twelfth lecture in the fourth series of his *Clinique des Maladies du Systeme Nerveux* is devoted to a case of progressive muscular atrophy of the Aran-Duchenne type. Under diagnosis the author says: "Il s'agit indubitablement d'un cas d'atrophie musculaire progressive." The autopsy showed (report published with the series of cases reported to the last International Congress in Paris, 1900, by Phillipe and Guillain) that the lesion was that typical of amyotrophic lateral sclerosis. When the case was examined by Raymond the exaggeration of the reflexes which had previously existed had disappeared.

There are cases of amyotrophic lateral sclerosis in which the spastic symptoms precede the atrophic manifestations, and others in which they predominate. Such cases bespeak an earlier or more profound involvement of the lateral columns than of the gray matter. Moreover, there are trustworthy records of many cases in which the degeneration of the pyramidal tracts was complete, while the process of the disease in the gray matter was still in a state of progression.

It is not easy to understand why there should be so much and such acrimonious discussion as to whether the gray matter or the white is first to be involved. In amyotrophic lateral sclerosis we are dealing with a poison or noxious influence which is capable of causing destruction of two distinct portions of the spinal cord which are rarely diseased simultaneously—the white and the gray matter. If this is admitted, why should not one of them be diseased first in one instance and the other in a second instance?

Whether amyotrophic lateral sclerosis is a part of or a variety of spinal progressive muscular atrophy is another question, and a question which, as I have indicated above, must, it seems to me, be answered in the negative. Although spinal progressive muscular atrophy may be accompanied by disease of the white fibres of the cord which on microscopic examination reveals itself as a degeneration of the supplementary zone, there is never any such degeneration of the pyramidal tracts as that ordinarily found in cases of amyotrophic lateral sclerosis. I do not recall that any case has been recorded in which degeneration of the central motor neuron throughout its entire extent existed. So that from a clinical as well as from an anatomical standpoint it seems the identity of these two diseases must be denied. A little later on we shall see that a consideration of the etiology leads to the same conclusion.

The clinical picture of amyotrophic lateral sclerosis is a very constant one, and liable to but slight variation. The symptoms are typified by the case reported in detail in this paper, so that they do not call for repetition here. In looking through the literature of the subject I have been impressed with the frequency with which mental symptoms have been observed. By this I do not mean cases in which the disease has developed in insane persons, such as in the case of Sarbo and of Dornbluth. Amyotrophic lateral sclerosis may develop in an insane person as well as in a person of sound mind. I am inclined to think that it is an error to classify such cases as that reported by Zacher as a typical form of the disease. A man of thirty developed six years after syphilitic infection disturbance of speech, and later the clinical picture of general paresis, which was accompanied with atrophy in the upper extremity. The autopsy, in addition to many other lesions, revealed changes in the crossed pyramidal tracts and slight alteration of the anterior horns. Nor do I think that such cases as the one recently

reported by Jurman as one of amyotrophic lateral sclerosis supervening in a general paretic after a blow on the jaw which caused a fracture should be included with this disease at all. Jurman's patient developed difficulty of swallowing and of speech, inability to put out the tongue, feebleness of the arms and legs, augmentation of the tendon-jerks, clonus of both feet, difficulty in walking, slight diminution of faradic irritability, and forced laughter. I can see nothing in a symptom-complex such as this incompatible with general paresis. Bearing in mind the widespread and extensive decay of neurons which characterizes general paresis, it is far more legitimate to classify such cases under that disease than to try to put them under the rubric of amyotrophic lateral sclerosis.

The mental symptoms of amyotrophic lateral sclerosis that are worthy of mention are suicidal impulse, such as existed in my case, attacks of meaningless laughter and of weeping without direct cause, occurring in an impulsive manner, and evidences of slight dementia. All of these symptoms may well have their foundation in the organic changes that go on in the brain. It is not improbable that the impulsive, uncontrollable emotional display bespeaks an involvement of the motor neurons extending into the thalamus. In a similar way such cerebral manifestations as those reported in a case by Erben, paraphasia and disturbance of speech and intelligence, may be attributed to disease of the corticomuscular neurons. The point that may be emphasized here is that mental symptoms occur with considerable frequency in this disease and rarely in spinal progressive muscular atrophy.

The Etiology of Amyotrophic Lateral Sclerosis. The etiology of amyotrophic lateral sclerosis is very obscure, practically nothing is known of the real cause of the disease, and I regret that I am unable to contribute anything. Whatever information is to be derived from a study of a considerable number of cases will, however, be here set forth. After careful examination of the entire literature of amyotrophic lateral sclerosis, I have selected the records of ninety-four typical cases and added to them ten of my own cases, five with autopsy and five without, and have made these the basis of a statistical study.[1]

Of the 104 cases 55 were males and 49 females. It will be seen at once that this is at variance with the statements of many previous writers regarding its frequency in the two sexes. The French school particularly are positive in their statement that the disease is much more frequent in females than in males. Probst, who made a careful analysis of 53 cases in 1898, found that the number was evenly distributed between males and females. As my cases are in nowise

[1] Dr. Joseph Frankel has kindly loaned me the histories of three typical cases, which are incorporated.

selected, merely taken from the literature wherever a typical case could be found, the inference is more reliable than from a small number of cases personally observed. For instance, of the last 7 cases that I have seen personally 5 were men and 2 women.

It is generally held (and I have heretofore shared the view) that amyotrophic lateral sclerosis is more frequent between the ages of thirty and forty. In 100 unselected cases 30 patients were between thirty and forty; 29 between forty-five and fifty; 28 between fifty and sixty, and 2 under thirty. This would seem to show that the decade following the forty-fifth year is equally liable to the affliction.

In 26 cases the total duration of the disease was fifty-five years, which makes the average duration a little more than two years. This coincides with my experience. The briefest duration of the disease in cases found in the literature was five months, and this patient was carried off by influenza. In 2 cases, however, the disease seems to have run its course in six months. Record of 4 cases was found in which the disease lasted only nine months. A few cases only lasted upward of five years; the longest on record seems to be ten years.

The part of the body to be first affected was inquired into with considerable interest. Out of 81 cases in which there was specific information on this point the upper extremity was affected first in 39 cases, the lower extremity in 14 cases, and the upper and lower extremity (hemiplegic), or all four extremities, in 11 cases, while the disease came on with bulbar symptoms in 21 cases. In upward of 50 per cent. of all the cases bulbar symptoms appeared within the first year. But in the cases that are ushered in with bulbar symptoms it is not long before atrophy or spasticity or both show themselves in other parts of the body.

Patients are very apt to attribute their symptoms or disease to influence or experience known to be deleterious to their health, such as exposure to the wet or cold. This is the case particularly when the seemingly attributable cause precedes immediately the appearance of the first symptoms. Exposure to cold and wet, overwork, strife, fright, and bodily injuries were enumerated as causative in 28 instances. In many of the cases on our list no attributable cause is given. Bodily injury was said to have preceded the first manifestations of the disease in seven instances; but the relationship of injury is often very remote, as in the following case:

J. E., aged forty-five years, shoemaker, married, born in Russia; dates the beginning of his illness to July, 1897. He attributes it to a fall from a car three months before, which, however, produced no apparent injury. He complains of weakness in the hands and feet and of difficulty in speech. He has had considerable vertigo, headache, and nervousness, and lately difficulty in swallowing and chewing has been noticed. He complains also of a "drawing" sensation in the legs and hands, of a sensation of coldness in the lower half of the abdomen, and

of heat in the upper half of the body, which is also the seat of profound perspiration. In September, 1897, an examination showed typical spastic gait, short, wooden stride, locomotion being accomplished with great difficulty. Fibrillary twitchings of the shoulder girdles are very conspicuous. The patient is unable to close the mouth tightly on account of fibrillary twitching of the face and weakness of the lip muscles. There is no atrophy.

On March 2, 1898, an examination was made, of which the following is a transcript of the notes:

The patient is of medium size, fairly well nourished, except in the localities where muscular atrophy has reduced the volume of the parts. The head inclines somewhat toward the right side, the eyelids are drooping, and the facial expression is immobile. There are no scars on the body, except one in the right popliteal region, the result of an intentional injury in order to avoid military duty. When the patient is raised the upper extremities are flexed at the first interphalangeal joints. The lower extremity is slightly flexed, and there is plantar flexion at the ankle-joints. Fibrillary twitchings are to be seen especially in the right upper extremities, in the muscles of the shoulders, and in the muscles of the mouth, they are present, but to a lesser degree in the muscles of the lower extremity, and here, too, they are more conspicuous on the right side than on the left. The patient is unable to whistle or to blow out the cheeks, and the mouth is characteristically tapir. The tongue is constantly in the state of undulatory movements, and is very much limited in its excursions without and within the mouth. There is considerable spasticity of both upper extremities, and the tendon-jerks are all exaggerated. The atrophy in the upper extremity is most profound in the extensor muscles of the forearms, and the thenar, hypothenar, and interossei muscles. In the lower extremities the thigh muscles on the right side are reduced in volume. Passive movements encounter marked resistance. The knee-jerks are lively, but there is no patellar or ankle clonus. The increase of tendon-jerks in the lower extremities is not proportionate to the profound spasticity. The plantar reflexes are lively. There is no disturbance of sensation or of the sphincters.

Electrical examination gives the following noteworthy information: To faradic and galvanic excitation the muscles at first showed rather increased irritability; this, however, is soon exhausted, and after the current had been applied a few times excitability is lost for a while. The transition is, however, not a sudden one, but it goes slowly from sharp contraction through various stages of vermiform contraction to entire absence of response. The ulnar nerves do not respond to any current.

Some cases of this disease attributed to injury, such as that of Goldberg, are reported so incompletely that neither the existence of amyotrophic lateral sclerosis nor the etiological connection of trauma is clear to the reader. In other cases, such as that reported by Oppenheim, in which the symptoms came on after severe overexertion, there existed symptoms (hyperæsthesia of the left thorax, anæsthesia for temperature, and pain in the right leg) which are never present in typical cases of the disease. On the other hand, there are cases, such as those of Strümpell and others, in which trauma seems to have been the imme-

diate antecedent of the appearance of the disease. Just how trauma acts to disease the motor neurons is not clear. Whether by the depreciation of mental and physical vitality or by the production of metabolic products which act injuriously on the motor neurons to facilitate the occurrence of the disease cannot be said. From a review of all the cases reported it may be said that trauma does not seem to be an adequate cause of the disease. Personally I have never seen a case in which I thought it had the slightest etiological influence. Overwork, and especially overwork of a particular character, such as that of gold-beaters, embroiderers, etc., which calls for exhausting use of certain sets of muscles and which plays a rôle in the etiology of spinal progressive muscular atrophy, does not seem to enter into the etiology of the disease under consideration. It occurs mostly among the working class, but no particular occupation would seem to stand in relation to it.

There is much in the natural history and occurrence of the disease which reminds one of an infectious or intoxication process, and it was with considerable interest that the list of cases that I have selected was looked through to determine if there were any information to be had upon this point.

A number of cases have been reported which developed within a short time after parturition. These may be dependent upon some unknown toxic substance. The following case is an excellent example:

Mrs. P. V., aged thirty-four years, born in Russia, married, and has six children, four of which died in early childhood, two are living and well. She has always had good health. Her present illness began a year ago, immediately after the birth of her last child. She arose the sixth day after a normal labor, and soon experienced an increasing weakness of all of the extremities. Within the next six months this had increased to such an extent that she was unable to get out of a chair or to help herself, as in eating and in dressing, with the upper extremities. There was no complaint of pain or of disturbance of the sphincters. She complains now, December 7, 1895, of a "tension in the nerves" (spannung), and of nervousness, of stiffness of the legs, and of paralysis of the four extremities. Examination at this time shows a woman of medium size, fairly well nourished, lying in bed. She is unable to stand, to sit, to work, or to make any movement except of the head, and limited movements of the upper extremities. The left upper extremity is weaker than the right. There is no difficulty in swallowing, but she says that it requires much effort for her to speak, and her voice is slightly husky. There is pronounced atrophy of the thenar, hypothenar, and interosseous muscles of both hands, more advanced in the right hand. Atrophy of both shoulder girdles, more pronounced on the right than on the left, and distinct fibrillary twitching in the atrophying muscles. The jaw-jerk is very lively, the elbow-jerks are increased, the knee-jerks are somewhat plus, the plantar reflexes are absent. There is no atrophy of the muscles of the lower extremities despite the motor paralysis, but fibrillary twitchings are noted from time to time in the muscles of the thigh. There are no sensory disturbances, the sphincters

are intact. The notes of examination, made six months later, are as follows:

The patient has become more helpless. She now has difficulty in swallowing, food frequently gets into the larynx, and liquids often regurgitate, and there is marked disturbance of speech. It is very difficult for her to speak at all when she is lying flat. Respiration is hurried and shallow, and the accessory muscles of respiration are constantly being called into play. The respiratory murmur is scarcely audible. The atrophy of the upper extremity has become more profound. Passive movement of the left shoulder meets with elastic resistance and is painful to the patient. She is still able to elevate the shoulders slightly and to flex and extend the right arm to a very slight extent. She can also make limited movement of the right toes. The atrophy, which involves the supraspinatus, deltoid, muscles of the forearm, the lumbricales, interossei, thenar, and hypothenar eminences, is very advanced on the right side. There is fibrillary twitching in all of the atrophic muscles. The response to galvanic current is sluggish and vermiform, the best contraction being obtained by the kathode. The galvanic reaction is lost in the peroneals, diminished in the nerves of the upper extremities. The faradic irritability is still present but very sluggish. The tendon-jerks are increased; there is considerable spasticity of the upper extremities, less in the lower extremities. The patient now has attacks of spasmodic crying and laughing.

Six of the patients gave a history of syphilis. This is probably not more than the actual percentage of syphilization. In two of these cases, both my own, there may have been some direct relationship between the syphilitic infection and the amyotrophic lateral sclerosis. A brief outline of these cases is as follows:

The patient, a single man, forty-nine years old; was by occupation a house and sign painter. He has never had lead poisoning. When forty-four years old he contracted syphilis, for which he had no treatment save local application. Two years afterward, without apparent or attributable cause, the muscles of the left hand began to atrophy. A few months later the atrophy began in the left leg, and about the same time he began to be slightly spastistic. The atrophy, which was in active progress at the time of his admission to the hospital, now involved both upper extremities, the left more than the right, and to a slight extent the left lower extremity. The tendon-jerks of the knees, ankles, and elbows are much exaggerated, the left more than the right. There is no ankle clonus. The patient complains of stiffness and a feeling of tension in the back of the neck. There are no sensory or sphincteric disturbances. Bulbar symptoms have not yet shown themselves.

In the second case the syphilitic element in the disease seemed to be of much importance. This case is clinically a typical example of amyotrophic lateral sclerosis. Still, it is not unlikely that the pathological process upon which it is dependent is a syphilitic disease of the spinal cord, syphilitic myelitis, if we wish to use that term, the brunt of the lesion being borne by the anterior horns with coincident or secondary

involvement of the white matter around them. It is probable that the pathological change in such cases begins in the bloodvessels and constitutes a syphilitic arteritis or endarteritis, and that the changes in the parenchyma are secondary.

A plumber's assistant, aged forty-eight years, contracted syphilis when thirty-six and received treatment until the local manifestations of the disease had disappeared, *i. e.*, for two or three months. He remained well until the end of August, 1902, when, while driving nails into a resistant wall, the left hand wielding the hammer, he experienced a sense of increasing powerlessness in the left upper extremity. He had to quit work, and has not returned to it since. The weakness of the left upper extremity continued to increase, and soon became manifest not only in the shoulder but in the forearm and hand, the flexors being particularly weak. Within a month he remarked some weakness of the muscles of the right forearm and hand, the two middle fingers being weakest. About six weeks after the onset of the symptoms he noticed for the first time atrophy of the muscles of the left shoulder girdle, and later of the muscles of the arm and forearm. Aside from the sensation accompanying fibrillary twitching in the atrophying muscles, the patient made no complaint.

Examination three months after the attributed onset of the disease revealed profound atrophy of the muscles of the left shoulder girdle, the biceps and triceps, and slight atrophy of the pectoral muscles. The flexor muscles of the left forearm are more atrophied than the extensors on the left side, while on the right side this condition is reversed. The tendon jerks are very much exaggerated all over the body. Myotatic irritability is slow. The plantar reflexes are very lively and of the flexor type. The abdominal reflexes are present, and the cremasteric diminished. There is some increased resistance to passive movements of the lower extremities. All forms of sensory stimulation are interpreted correctly. The pupils are reduced to a pin-point and dilate very slightly in the dark.

There are a number of cases similar to this recorded. In some of them the diagnosis of subacute poliomyelitis has been made on account of the rapidity with which the symptoms came on, or because of rather sudden accession to the symptoms. The explanation of such abruptness is, I believe, that one or more diseased bloodvessels ruptured and caused rapid destruction of surrounding nerve cells. I would not be understood to say that I consider these cases genuine examples of amyotrophic lateral sclerosis. The point that I wish to make is, that there are cases of syphilitic disease of the cord (best designated at the present time as focal myelitis) which parallel the symptoms of amyotrophic lateral sclerosis, in the beginning at least, very closely, and that these may be called syphilitic amyotrophic lateral sclerosis.

In the first case the patient's occupation may have had something to do with the development of the disease, for there have been cases recorded in which lead poisoning would seem to have had some relationship to the development of the disease, as in the following case:

A house painter, thirty-five years old, of good habits, and who denied syphilitic infection, gave the following history: Four years before the onset of his present symptoms he had a typical attack of painter's colic, from which he recovered in a fortnight, since when he has kept at his work. A year ago he first noticed weakness of the little finger of the right hand. Soon after the atrophy became evident, not only in the hand, but in the right shoulder girdle. The atrophy was accompanied with marked fibrillary twitchings, "cramped" feeling in the arms, and pain and stiffness of the neck. The knee-jerks, ankle-jerks, and the triceps-jerks are exaggerated, and there is an atypical Babinski reflex. Bulbar symptoms have not yet shown themselves.

In a case of this kind it may be a mere coincidence that the disease occurred in a worker with lead. But knowing, as we do, that lead has a special predilection to attack motor neurons, it may well be that it bore some relationship to the immediate development of the disease in this case. In fact, it may be said that all of the factors that have been attributed as in some manner causative of the disease, such as injuries, exposure, intoxications, and the like, act only as the fuse to ignite the pile that is already prepared. Back of it all is the *something* which is the real cause of the disease.

Finally, a great deal has been written about an innate disposition on the part of the neurons to undergo degeneration when subject to influences which would be innocuous to properly endowed and developed neurons, an abiotrophy of the motor neurons, to use a term recently introduced by Gowers. It must be admitted that the tissues are endowed with a certain vital resistance, and when this wanes off they readily fall a victim to injurious influences, but amyotrophic lateral sclerosis has, in the main, the clinical features of an active destructive disease, not a decay. Although I am willing to admit prenatal influences, there must be some more tangible and actively operative cause. It is not unlikely that we must look to the pathological chemist for the discovery of the real noxious agency.

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CONGENITAL DISLOCATION OF THE SHOULDER.

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Congenital dislocation of the shoulder is of infrequent occurrence, and recorded cases of this affection are still very few in number and some of them are of doubtful value. Instances are recorded in adults and it is only on more or less certain commemoratives that the congenital nature of the condition has been diagnosed. Other cases have been met with in the fœtus, but in these a detailed account is wanting.

I have endeavored to collect all reported cases of congenital dislocation of the shoulder, but there are only a few that are really conclusive.

Many of them appear to me simply traumatic dislocations occurring during delivery, and in these cases the condition is usually a separation of the epiphysis, while others are instances of infantile paralysis. Still others are simply a diastasis due to a relaxation of the ligaments; while still others appear to have a distinctly congenital origin, which is proven by an electrical examination of the muscles or by post-mortem examination. In this paper I shall deal only with the two latter conditions.

The history of congenital dislocations goes back to Hippocrates, who speaks of them in several passages of his writings, but since his time the attention of surgeons was nearly turned away from this congenital defect until that great master, Ambroise Paré, again called attention to this type of lesion, although he appears to have had the traumatic obstetrical type more in view, for he says: "Car souventes fois les luxations arrivent aux enfantements difficiles quand les sages-femmes, tirant les bras des enfants, disloquent les iouointures de

l'espaule ou de la cuisse." From this time on little seems to have been written on the subject until William Smith contributed an article in 1839 in the *Dublin Medical Journal*, and again in 1847 in his *Treatise on Fractures*, this author publishes two cases of his own. In 1841 Gaillard published a case of congenital dislocation of the shoulder in the *Mémoires de l'Académie de Médecine*, which, unfortunately, like many others, was not proven by an examination of the periarticular muscles, but which, nevertheless, may be included in the congenital form on account of the deformity of the articular ends, which was easily demonstrated because of the extreme thinness of the tissues of the patient. At about the same time—that is to say, in 1841—J. Guerin considered the question more fully and admitted three varieties of congenital dislocation of the shoulder, namely, (1) directly downward, (2) downward and inward; (3) outward and upward. He quotes several examples upon which he based this division, but only one appears to me as demonstrated, and this was a fœtus presenting a subdislocation of the humerus outward and upward.

A few years later Bouteillier published, in the *Bulletin de la Société Anatomique* of 1849, a case of congenital deformity of the shoulder in a patient afflicted with Pott's disease. At the same time Cruveilhier wrote in his *Traité d'Anatomie Pathologique* the following passage: "Il faut bien se garder de confondre avec les luxations congénitales de l'humérus de simples diastases par relâchment des ligaments, telles que la diastase de l'articulation scapulo-humerale dans le cas de paralysie du deltoide. . . .

"Sur six cas présentés par Smith, il n'y en a que deux qui présentent une double luxation (luxation symétrique); seuls, ces deux cas ont été l'objet de dissection, et peuvent, par conséquent, être pris comme preuve a l'appui.

"Dans les autres cas, on s'est basé: (1) d'apres les commémoratifs, ni les malades ni leurs parents ne se rappelant aucune violence extérieure dirigée contre l'épaule; (2) d'après les signes cliniques fournis par l'examen de l'articulation.

"Voici, d'ailleurs, la description détaillée d'un fait que j'ai eu l'occasion d'observer et que je crois appartenir a une luxation congénitale de l'humérus dans la fosse sous-scapulaire. *Il serait cependant possible qu'il dût être rapporté a une diastase consécutive à une paralysie musculaire.*"

Alphonse Robert wrote a thesis in 1851, entitled *Des vices congenitaux de conformation des articulations*, in which he reviews those cases which had been published on the shoulder-joint and mentions those that have already been alluded to. But the most important contribution to the study of congenital dislocation of the shoulder that had appeared up to that time was a thesis upheld at Paris in 1866 by

Leonidas Loignon, and in this work the author had carefully collected twenty-four cases of dislocation of the shoulder, among which only a small number could be classified as congenital. Meyer reports an interesting case and also states that d'Outrelepont had told him that he had seen a dead-born fœtus at term which had a double dislocation of the shoulder. The labor had been an easy one. A projection of the acromion and an infra-acromial depression were noted, while the head of the humerus was found under the coracoid apophysis. The shoulder and the arm were less developed than on the opposite side.

In 1879 Jenni reported a case of congenital dislocation of the left shoulder, and in the same year Küster recorded an instance of a one-year-old child presenting a congenital backward dislocation of both shoulder-joints. Nothing more appears to have been written on the subject until about 1895, when Phelps commenced to write on the lesion. Another case was reported by Lewis, of Philadelphia, in the *Medical News;* then in 1898 two others were published by Scudder, of Boston, in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, one by Eve, of London, while the latest contribution that I have been able to find appeared in 1901 in the *New York Medical Journal* from the pen of Dr. Marsten, of New York. I would say, however, that Kirmisson, in his *Traité des Maladies chirurgicales d'origine congénitale,* devotes a short article to dislocations of the shoulder, and after remarking that the affection is of extreme rarity, the greater number of instances being due to a paralysis or to a traumatism inflicted during birth, he admits three varieties, namely, (1) subcoracoid, (2) supra-acromial, and (3) infra-acromial and infra-spinous. He also says that he has met with a congenital infra-acromial dislocation in a girl aged fourteen years; the arm was atrophied and shorter than its fellow, while the movements of the shoulder, more especially that of elevation, were very incomplete.

The etiology and pathogenesis of congenital dislocation of the shoulder-joint are most obscure, and many are the opinions that have been emitted by various authorities, but there is not one that gives entire satisfaction. It is far from my intention to make the pretention of adding a new theory to those already existing, and I simply propose to examine the principal ideas which have already been emitted and discussed regarding the subject of congenital dislocations in general.

Now, in the first place, a point that strikes one's mind most forcibly in the study of the etiology is the greater frequency of congenital dislocation in girls than in boys, and this predilection for the female sex is most difficult to explain. It has been upheld that the skeleton of woman and those of man did not have exactly the same disposition; but, nevertheless, at the beginning of life it appears to me that the same dispositions exist in the same degree in both sexes.

In considering the subject of congenital dislocations of the hip, Roser formulated an hypothesis according to which the testicles are the starting-point of reflexes which prevent the fœtus placing his lower limbs in positions which would be favorable for the displacement of the head of the femur. Although this hypothesis is quite suggestive, it does not explain what cause may prevent unfavorable positions in the other limbs, and particularly the structures composing the shoulder in male infants. It is, nevertheless, a fact, which has been amply demonstrated by Broca, that congenital dislocation of the hip occurs in male children in 80 per cent. of the recorded cases.

Another fact which is interesting, and to which I believe no satisfactory explanation can be given, is that congenital affections are more frequently met with in girls belonging to the lower classes than in those born of well-to-do parents. I think that in the case of congenital dislocations intra-uterine rickets may possibly play a certain rôle.

There is another etiological factor besides the question of sex that is most important to consider, and this is heredity. Geoffroy Saint-Hilaire has said that in all ages it has been known that parents often transmit anomalies of organization with which they may be affected to their descendants, just as they transmit their physical constitution or their moral and intellectual qualities. Sometimes the father or the mother only give this unhappy heritage to the children, either of their sex or of the opposite, while occasionally, on the other hand, they transmit the deformity equally to the children of both sexes, and the ills of one individual thus become the common property of an entire race. Occasionally even a perfectly formed normal subject, but who was the issue of ill-formed parents, will see the anomalies which afflicted the latter reappear in his children.

In order to explain the existence of hereditary deformities a primordial defect in the organization of the germs has been admitted, and these congenital defects, according to this theory, are due to an aberration in the formative force—in other words, to a disturbance arising in the process of formation. It often happens that the ends of bones composing a joint have an abnormal form or direction from which a malformation of the joint ensues.

Alcoholism, tuberculosis, and syphilis in the parents or ancestors have often been accused of producing congenital deformities, and from the light that has been thrown on this important subject by modern researches in embryology, it would appear to me that these are potent factors. Other than the two circumstances already mentioned, namely, the much greater frequency in the female sex on the one hand, and heredity on the other, which at the present time are certainly above discussion, absolutely nothing is known regarding the etiology of congenital dislocations.

The pathogenesis of congenital dislocations is a much discussed question, and has given rise to numerous and dissimilar theories. The oldest one, which goes back as far as Hippocrates, considers congenital dislocations as due to an intra-uterine trauma, and although this explanation is far from satisfactory, it has been upheld by J. L. Petit and Cruveilhier. In 1876 Preuss, in considering the etiological part played by trauma occurring to the mother during pregnancy, reported a case of a woman in the fourth month of gestation who fell on a hard object, striking on the left side of the abdomen. She gave birth to a lusty boy, who presented an irreducible dislocation of the humerus and a fracture of the forearm which had united with the formation of a bone callus. This authority at the same time pointed out the bad influence exerted by dress, riding, dancing, and heavy work during pregnancy. But this theory does not explain why the dislocation occurred, and still less why the dislocation is often a double one, and for that matter no anatomical fact can demonstrate the effect of a trauma upon the production of a congenital dislocation.

The second theory which attributes a congenital dislocation to a disease of the joint of the fœtus during intra-uterine life has no foundation whatever. Hypertrophy of the adipose tissues between the articular surfaces, tubercular arthritis, and hydrarthrosis, with a consecutive relaxation of the ligaments, have all in turn been incriminated as factors in the production of congenital dislocation. But the trouble is that these diseases have never been anatomically demonstrated, and Lorenz has said that in opening such joints he has never been able to find an increase in the quantity of the synovial fluid.

In 1890 Pfender endeavored to demonstrate that congenital dislocations were a manifestation of hereditary tuberculosis; but he only succeeded in proving one thing, and that is that tuberculosis is very frequent and that it does not prevent a child from having a congenital dislocation.

Besides traumatism, or any other affection of the fœtus during pregnancy, J. L. Petit, d'Outrelepont, and others, have stated traumatism during labor as a cause; but in point of fact this theory is not acceptable, because not only in several cases the obstetrician was not obliged to interfere; but the researches of Duchenne, Vallette, Lorenz, Krönlein, Loignon, and Hofmokle, regarding traumatic dislocations in the newly born, have demonstrated that according to the anatomical conditions a fracture or a separation of the epiphysis will take place under the action of external violences, such as torsion or traction, but that dislocation never results.

The fourth theory has been advanced by Jules Guérin and Verneuil, who believed that every congenital dislocation was due to a pathological condition of the muscles, resulting from an infantile paralysis. For

both these authorities the cause of the dislocation was a loss of muscular equilibrium; but, contrary to Guérin, Verneuil denied that muscular contracture played any part in the production of these lesions.

From the cases reported in the literature including my own, I think that it is easily proven that a congenital dislocation may occur without any symptom of infantile paralysis being present, and in my own case, as well as from one recorded by Picot, it will be observed that all the electric tests were preserved in all the muscles surrounding the shoulder-joint, and, consequently, all possibility of a myelitis could be eliminated.

The last theory, which is due to von Ammon—the so-called theory of arrested development—remains to be briefly considered. This authority includes this malformation among the congenital articular dystrophies. This theory, however, has undergone many changes from those who have studied it. There are some who believe that a congenital dislocation is due to an absolute absence of parallelism in the development of the joint cavity and the head of the bone which it is intended to receive. In other words, this simply means a disproportion between the container and the contained.

Other authorities recognize the fact that in reality the lesions are far more complicated, and that they not only occur in the joint cavity, but on the articular extremity of the bone as well, so that all the elements entering into the formation of the joint participate in the deformity.

This latter theory is perhaps the most acceptable, and explains why heredity may be one of the most important etiological factors in the production of these deformities; but, nevertheless, it must be said that the study of etiology and the pathogenesis of congenital dislocations has not made much progress since the time of the writings of the great physician of Cos, and still remains a most obscure question.

The pathological lesions found in congenital dislocation of the shoulder are pretty much the same in all the recorded cases, and what is most striking is the arrest in development of that portion of the skeleton upon which the muscles take their insertions. The muscles, too, are atrophied. The capsule of the joint is intact, and its insertions are normal. It is only somewhat relaxed, very distended, and occasionally considerably elongated.

If we consider those cases which have been examined necroscopically, it will be noticed that an arrest in the development of the bones forming the shoulder-joint is noted in all. In Bouteillier's case the shoulder was badly formed, the articular cavity was almost filled up and its cartilage was wanting; the humerus was slender and inflected, while its head was flattened.

In both cases recorded by Smith the glenoid cavity was reduced to

about one-third its normal size, while its internal border was completely wanting; the humerus was thin and atrophied, while its head had an oval shape, the largest diameter being vertical. In Mayer's case the glenoid cavity had completely disappeard, while the head of the humerus, which was oval or rather oblong in shape, was in direct contact with a newly formed cavity which had been produced from the border of the glenoid.

Cruveilhier found a glenoid cavity and apophysis forming a flattened stump, deprived of cartilage and directed outward; the head of the humerus was greatly deformed, and the small trochanter projected markedly. In all cases the capsule was found intact and presented its normal insertions on the bone. In my own case and that of Bouteillier it was very much distended.

In most cases the muscles were found generally atrophied, but this atrophy was due to a decrease in the number of fasciculi, and consequently was a true atrophy due to a formative defect and not from degeneration. It is the same arrest of development as is found in the extremities of the bones, and from this it results that certain muscles are shortened while others are elongated, according to the new position that the head of the humerus occupies in the articulation.

For the same reason the bloodvessels and the nerves may be altered and shortened; but although this shortening is of no great consequence for the bloodvessels on account of their elasticity, it has its importance for the nerves, whose functions might be badly disturbed if brutal manœuvres in the reduction of the dislocation were undertaken.

When we are dealing with a malformation of the shoulder-joint, we should consider two things: First, the recognition of the congenital nature of the disease, and, second, if such be the case, the structures entering into the formation of the joint should be carefully examined. The congenital nature of the affection is not always an easy matter to decide, because oftentimes the diagnosis can only be based on the commemoratives of the parents. The general aspect of the deformed shoulder rarely indicates the affection with which one is dealing, and for this reason the question of heredity and personal antecedents of the patient should never be neglected.

It is quite natural that if in the ascendants of the patient several of them are found to have had similar conditions, or if in the patient two or more malformations are also present, it is most probable that the condition is a congenital one.

Many errors have been committed, and I would mention as instructive one that was made by Nélaton in a case diagnosed as a congenital dislocation of the shoulder. The patient died and at the necropsy lesions of the circumflex nerve and the cervical portion of the cord were found.

The principal character which will allow one to distinguish a congenital origin from an accidental affection may be stated as follows, namely, that a congenital dislocation is usually easy to reduce, but very difficult to maintain reduced; while in the case of an acquired dislocation reduction is almost always impossible, but if it can be accomplished the parts are easily retained in place. In Picot's case all that was necessary was to seize the left arm and give it a slight rotation outward, and the head of the humerus was reduced without difficulty; but as soon as the arm was liberated, the head of the bone immediately returned to its former position. Jenni treated his case by a prolonged extension with rotation, and the dislocation recurred ten times. In my own case reduction could be partially accomplished under ether, but the parts would not remain in place.

Continuing the question of diagnosis, I would point out that two circumstances must be distinguished, the first being relative to the length of time after birth that the subject is examined, whether it be at the time of birth or a few days afterward, or when the child has attained several years or more.

If we examine a child at the time of birth or within a few days following, we may be simply dealing with an intra-uterine traumatism, in which case the commemoratives will be of great assistance. The etiological action of intra-uterine traumatism is not absolutely proven, and in the cases that I have collected this accident has not been met with during the pregnancy.

On the other hand, we may be dealing with an obstetrical traumatism. It is well known that a traumatic dislocation during labor is extremely infrequent, and that it is in most instances in reality a fracture of the upper end of the humerus or a separation of the epiphysis. Under these circumstances, besides the absolute impotency of the fractured limb, a painful tumefaction will be found around the joint. The search and manipulation is not an easy thing to carry out in a very small baby, but if gentleness and perseverance be employed, the painful region may be quite exactly mapped out and occasionally a very slight crepitation may be elicited, and there will be found a more or less extensive ecchymosis.

These symptoms are wanting in congenital dislocation of the shoulder, in which case the joint is perfectly free and all symptoms of an inflammatory process are lacking. Congenital dislocation of the shoulder may also be confounded with a congenital relaxation of the articular ligaments; but in this case the dislocation is not present when the limb is in repose, but it is produced with the greatest ease when any slight effort to use the arm is made. After reduction the parts remain in place.

Obstetrical paralysis is characterized by its usual location in the

deltoid, infraspinous, and flexor muscles of the forearm. The arm hangs down in internal rotation and lies against the thorax, while the hand is in pronation and the fingers flexed. Since the deltoid muscle is always involved in root palsy, the shoulder is depressed, immovable, and the arm cannot be raised. Nevertheless, since the trapezius is not involved, this muscle may give a few feeble movements to the shoulder.

Sensibility is completely preserved in the entire extent of the upper limb, but if the electric reactions of the paralyzed muscles be studied, it will be found that they do not respond to the faradic current, or, if they do, it is only faintly. In the beginning, at least, they do react to the galvanic current.

What distinguishes most positively a congenital dislocation of the shoulder from the paralysis is the preservation of the functions of all the muscles of the joint and their distinct excitability to electricity. In my own case, as well as in some others, all these reactions were present, and it is most unfortunate that in the other reported cases this part of the examination has been neglected.

Congenital dislocation of the shoulder may be differentiated from syphilitic pseudo-paralysis, inasmuch as the latter disease hardly ever makes its appearance before the first or second month after birth. It also coincides with more or less advanced lesions of the bones, as well as with cutaneous and mucous manifestations of syphilis, while a dislocation, on the other hand, dates from birth and there is an absence of syphilitic stigmata.

We should also bear in mind the differential diagnosis between dislocation and a paralysis having a cerebral origin; but in the latter condition the paralysis is only exceptionally monoplegic. In most instances it takes on the hemiplegic type and includes both upper and lower limbs and the inferior facial nerve.

In those cases where the child has already attained several years in age, we will, in the first place, be obliged to eliminate all the ordinary lesions which affect the joints. Acute articular rheumatism is characterized by a periarticular swelling, with a more or less acute pain on pressure. Spontaneous pain is also present and is frequently accompanied by fever. In congenital dislocation of the shoulder pain and swelling are absent, but there may be present some faint intra-articular cracklings which possibly might be mistaken for rheumatism. Generally considered, however, the symptoms are too evident to be misleading.

An old tubercular infection of the shoulder resulting in a spontaneous dislocation is a very rare condition, but its existence has been admitted by good authorities. The differential diagnosis is quite difficult, because it occasionally happens that the affection is cured without

leaving any external traces, and that the movements of the dislocated shoulder may in certain cases be quite as limited as those of a joint affected with an old white swelling. The presence of cicatrices resulting from former abscess formation will greatly aid in settling the diagnosis. The difficulties, however, become greater if we are dealing with a tubercular lesion occurring in a congenitally dislocated shoulder, and in this case we can only be guided by the commemoratives relative to the former condition of the joint.

Traumatic dislocations are of an extreme infrequency, and usually such cases are in reality either a fracture of the upper end of the humerus or a separation of the epiphysis. All young children are exposed to these affections, but after the age of two years they become more infrequent, while past the age of ten years they are exceptional. In cases of doubt radioscopy must be resorted to.

Progressive spinal amyotrophy of infancy can be recognized by the fact that it begins during the first year of life, denoting its presence by a paresis with atrophy of the muscles of the thigh and buttocks, and absence of symptoms of infection. It successively reaches the vertebral muscles of the neck and scapula, the arm and the forearm; then the muscles of the leg, the hands and the feet become involved. The progress of the atrophy is progressive, chronic, and symmetrical. Electric excitability is diminished and the reaction of degeneration is always present.

In the juvenile type of progressive muscular atrophy an error in diagnosis of congenital dislocation of the shoulder can hardly be made. Erb's disease appears either during early infancy or in young children, occasionally at puberty. Its commencement is insidious and shows itself as a weakness of certain muscles of the shoulder and arm, which can be detected when certain movements are made. The affection is always accompanied by a more or less apparent loss of flesh.

The muscles that are at first attacked are generally the pectoralis major (excepting in its clavicular portion), the pectoralis minor, the lower fasciculi of the trapezius, the dorsalis major, the rhomboids, the biceps, some of the muscles of the neck, the anterior brachial, and the supinator longus. Some groups of muscles are nearly free from the atrophic process, such as the sternomastoid, the coracobrachial, deltoid, the infraspinous and supraspinous, the muscles of the forearm, excepting the long supinator, and the thenar and hypothenar muscles. Electric excitability is proportionately diminished to the degree of atrophy present, while the reaction of degeneration is not distinct.

Landouzy-Dejerine type of paralysis is chracterized by a paresis and atrophy of the muscles of the face, shoulder, and arm. This myopathy occurs during early infancy and usually begins in the muscles of the face. The projection formed by the deltoid is replaced by a depression

through which a subdislocation of the humerus may be made out. This subdislocation is due to a relaxation occurring in the elements constituting the shoulder-joint. As the disease progresses the pectoralis major, the trapezius, the sternomastoid are each included in the process and undergo atrophy which contrasts very greatly with the normal condition of the muscles of the forearm and the hand.

Infantile spinal paralysis has often been accused of producing dislocation of the shoulder, and some have even gone so far as to deny the possibility of a congenital dislocation of the shoulder, believing that such a lesion was due to infantile paralysis. This disease is more frequently met with in early infancy, although infrequently it may occur later on in life. It begins suddenly with convulsions, cerebral symptoms, and temporary contracture. At the same time a fever, which lasts from one to eight days, makes its appearance, occasionally with remissions.

The disease attacks at once all the muscles that are to be affected. After this regression takes place and certain paralyzed muscles recover their electrical and voluntary contractility, while others remain paralyzed and undergo a progressive atrophy.

A congenital dislocation is noticed immediately after birth, and there is a complete absence of fever. All the muscles have their voluntary contractility, while their atrophy is usually due to the long inactivity to which they are subjected. Of course, certain movements are rendered difficult on account of the mechanical obstacle formed by the dislocated head of the humerus; but when reduction has been performed, the functional impediment seems to disappear.

In infantile paralysis muscular contraction to electric stimulation is notably diminished, if not completely absent, and the reaction of degeneration is always present. This research is most important and should remove all doubts as to the diagnosis, because in a true congenital dislocation all the muscles contract normally to the faradic and galvanic currents, and the reaction of degeneration is always absent. The prognosis of a congenital dislocation is not so serious as the monoplegic type of infantile paralysis, and if a careful study of the structures composing the joint is made, as well as of the muscles of the shoulder, in a large majority of cases that which belongs to a congenital condition and that which belongs to infantile paralysis can usually be made out. In all cases the muscular reaction and the presence or absence of the reaction of degeneration will allow one to make a correct diagnosis. I would say, however, that occasionally the fever usually observed in infantile paralysis may be absent. It also happens that the paralysis forms the first symptom. It may come on slowly and gradually increase, and then may slowly disappear without leaving any trace. Then the symptoms may reappear during the period of regres-

sion and the paralysis will extend to the bulb, resulting in death of the subject.

The condition of the ligaments of the shoulder-joint should be carefully examined, and it will be found that the changes that they have undergone almost always combine with the changes which have taken place in the bones. If the capsule is relaxed, the limb is very loosely hung, and the extent of its movements is considerably increased. If muscular action does not prevent, the head of the humerus may be displaced in all directions. If, on the contrary, the ligaments are shortened, they will prevent the movements of the joint, which will then be only partial.

The condition of the bones is not always an easy thing to ascertain, and in order to come to some conclusion the limb should be moved in all directions in order to explore the entire joint. The X-ray might be thought to be of value, inasmuch as it allows one to directly examine the condition of the joint; but if I had not made my clinical diagnosis of congenital dislocation of the shoulder before the radiograph was taken of my case, I believe that I should have been quite at a loss to know the exact condition of affairs had I been solely guided by the photographic picture of the skeleton.

The early methods of treatment which were applied to these cases practically consisted in a forced traction during a longer or shorter period of time, and immobilization of the joint after the dislocation had been reduced. From these considerations and also from what we know of the treatment of congenital dislocation of the hip, the following treatment may be employed if we are dealing with a very young child or a baby: hydrotherapy, cold affusions, massage, and electricity, which will keep the muscles well nourished, will certainly render considerable service; but with this a relative repose, and not an absolute one, should be given to the limb in order to prevent overfatigue and any action which might tend to draw the head of the humerus out of the cavity.

It would appear, however, that in the vast majority of cases the only satisfactory treatment will be surgical interference, and I propose here to briefly describe the operative technique for the reduction and permanent maintenance of congenital dislocation of the shoulder. The first operation that will be referred to is that advocated by the late Dr. A. M. Phelps, of New York, and is the one which was employed in the case here appended; but I would add that in my hands it was entirely unsatisfactory, inasmuch as the posterior incision made does not render the parts so accessible as if the joint were cut down on anteriorly, and for this reason other methods will be briefly described which will, I think, render the successful result of the operation an easier matter to attain.

Phelps' technique consists in an incision carried along the posterior border of the deltoid muscle, curving it downward. This gives a flap which its originator claimed readily exposed the head of the bone; but this is really far from the fact, as the joint is reached with difficulty. The capsule is then incised, and the head of the bone will be found under the spine of the scapula. It is stated by Marsten and Phelps that it is necessary to cut away about two-thirds of the head of the bone, or, in other words, down to the epiphyseal line. The bone should be rounded off like the original head, and then slipped into the glenoid cavity. The entire new articulation which has been formed by the head of the bone is next excised with a chisel or curette. The redundant capsule is then cut away and the capsule closed with catgut sutures. The limb should be put up in plaster, with the elbow well back and the arm at a right angle with the body.

A criticism that I would make is that from most recorded cases where operation has been undertaken, excision of the head of the humerus seems an unnecessary addition, for in these cases, including my own, the joint cavity and head of the bone were not sufficiently changed to necessitate any operative measures directed to the reduction.

That the capsule will always be found stretched or elongated is probably quite true in the majority of cases, and it is quite proper to reset enough of the capsule so that when it is stitched together it will cover the head of the humerus in a physiological manner.

There has been a large number of methods described and employed for gaining access to the shoulder-joint; three especially have been used. Langenbeck advocated the axillary region because it was more direct, since the head of the humerus is quite superficially located in the axilla and, consequently, easily attained. But this advantage is insignificant if one takes into consideration the many inconveniences that this incision presents, when it is essential to recognize and overcome the cause preventing reduction. There is also some danger of wounding the nerves and the vessels in this region, and on account of many other operative difficulties that have been reported by able surgeons this method has been more or less abandoned.

The posterior route has been particularly advocated by Nélaton and also, as we have seen, by Phelps. This is certainly an improvement over the axillary method. Nélaton's technique consists in making a horizontal incision on the external border of the acromion, and to this incision another one is joined at the posterior tip, directed downward toward the arm and following the direction of the muscular fibres of the deltoid (Fig. 1). By this combined incision a large cutaneous muscular flap is formed, which when thrown back gives a ready access to the posterior aspect of the region of the shoulder. It would, however,

appear that this posterior incision is in no way preferable to an anterior incision, especially if a forward dislocation exists.

On the contrary, with the anterior incisions this difficulty no longer exists, because the joint is attacked directly at the most desirable point. The technique that seems to me the most recommendable is that indi-

Fig. 1.

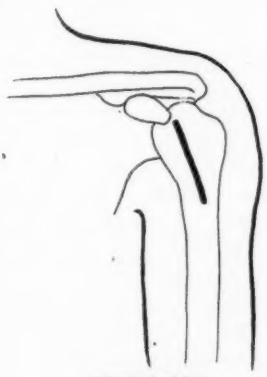
Nélaton's incision.

Fig. 2.

Duplay's incision.

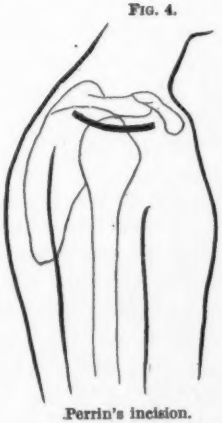
cated by Duplay, and is as follows: A horizontal incision is made over the external border of the acromion and is begun just within the acromio-clavicular joint, and carried backward to the origin of the spine of the scapula. A second incision starts from the anterior tip of

Fig. 3.



Ollier's incision.

Fig. 4.



Perrin's incision.

the first one and is carried downward and outward, following the direction of the fibres of the deltoid muscle, to which it runs parallel. The upper lip of the horizontal incision is dissected off as far as the acromion, and the external end of the clavicle is exposed. The acromion

is then sawn through at the point of continuity with the spine of the scapula, and the clavicle is then cut through in the neighborhood of its articulation with the acromion. The deltoid thus becomes mobilized with its upper insertion, and may, consequently, be pushed aside so that the shoulder-joint is freely exposed. Such a free operation may not always be necessary, in which case Ollier's anterior incision may be employed, as seen in Fig. 3; but as this is well known, a description of the technique seems unnecessary.

The incision proposed by Perrin, Demons, Senn, and others is horizontal and transverse. It is commenced at the border of the acromion, passes 5 millimetres below the point of this apophysis, and is carried directly to the point of the coracoid. The deltoid is incised in the same direction and pushed downward by a retractor. By this means the fibrous tissues opposing the reduction of the head of the humerus are exposed. Although this method has been employed with success by some operators, I cannot believe that it will ever become popular.

P. H., aged five years, was brought to me for a lesion of the right arm, which was noticed for the first time several days after his birth.

Regarding alcoholism, syphilis, or tuberculosis in the family, all was negative, and there were three other children, one older and two younger than the patient, who were in every way perfectly developed. The mother only did her housework and had received no injury during pregnancy. The father was a healthy man, and had never had any serious sickness. Nothing was noted in the history of other members of the family.

The child was born normally at term, without forceps. He was well built; but a day or two after the birth it appeared to the mother that there was something wrong with the right arm, as the child appeared to lack the use of it. When the hand was seized and the arm raised, it would fall immediately upon being released. When moved it did not seem to cause pain, as the child did not cry, and it was noticed that when left alone the arm was not endowed with any spontaneous movement. The physician of the family consulted at this time did not appear to have examined the arm, and simply recommended the use of a sling. As the child grew the movements of the limb began to appear, but were limited; those of the hand and of the wrist and elbow only appeared to be normal. An impotency of the shoulder-joint has been present, so that the child could not reach his mouth with his hand, and was obliged to bend the head forward in order to touch his lips.

Examination of the patient showed a well-formed boy. He walked perfectly well, and the left arm was functionally normal and anatomically was perfect.

Examination of the diseased limb showed a marked difference between the left side and the right. The anterior aspect of the right shoulder had lost its rounded form and appeared less broad, while the distance separating the internal extremity of the clavicle and the projection of the stump of the shoulder was shorter than on the normal side. The height of the axilla was also diminished, and the subclavicular hollow

was more accentuated on this side than on the left. The points of both scapulæ projected distinctly backward, and on the right the point of the bone projected very distinctly. On the right the internal border of the scapula approached the spinous apophyses, and from the fact of its ascension the right scapula appeared as if atrophied; but this was simply an illusion, because by measurement it was found to be identical on both sides in both its vertical and horizontal diameters. Movements given to the right arm were transmitted to a great extent to the scapula. Inspection of the posterior aspect of the shoulder showed an abnormal projection just below the base of the acromion.

FIG. 5.

When left alone the arm hangs by the side of the body in slight abduction, the elbow being about 6 cm. from the thorax. The limb is in very marked internal rotation. The anterior aspect of the elbow has become internal, and faces the thoracic wall, while the epicondyle is directed forward and the epitrochlea backward, and the olecranon.

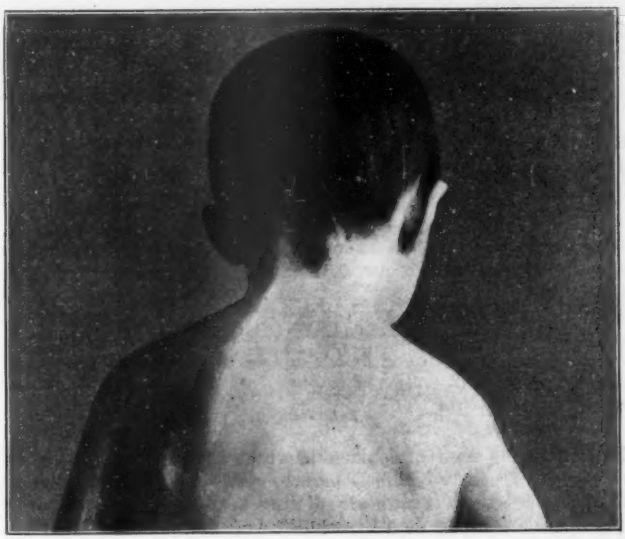
By palpation the external end of the clavicle and acromion are easily made out, under which a very depressible hollow is found which increases when the limb is abducted. Somewhat forward and below the acromio-clavicular vault a bony projection can be distinctly felt, recalling the shape of the coracoid apophysis. Over the posterior projection one feels that the teguments are pushed up by a bony projection of a

rounded form, and which participates in the movements given to the lower end of the humerus. This projection, on account of its shape, size, and mobility, impresses one as being the head of the humerus.

As to motion, abduction can be accomplished to quite an extent, but during this movement the arm is carried forward and cannot be projected backward. With the greatest effort the boy cannot raise his hand to his mouth or neck. Sensation is intact throughout the entire right arm, and trophic disturbances are wanting. Both radial arteries give a beat equal in strength and synchronous, so that any suspicion of vascular compression of the diseased side is eliminated. Electrical examination of the muscles shows that the periarticular muscles have preserved their reaction to both the faradic and galvanic current. Reaction of degeneration is absent, and the muscles are not contracted, showing that infantile paralysis is out of the question.

My diagnosis was congenital dislocation of the shoulder-joint, and in order to complete the diagnosis a radiographic picture of the thorax and both shoulder-joints was taken.

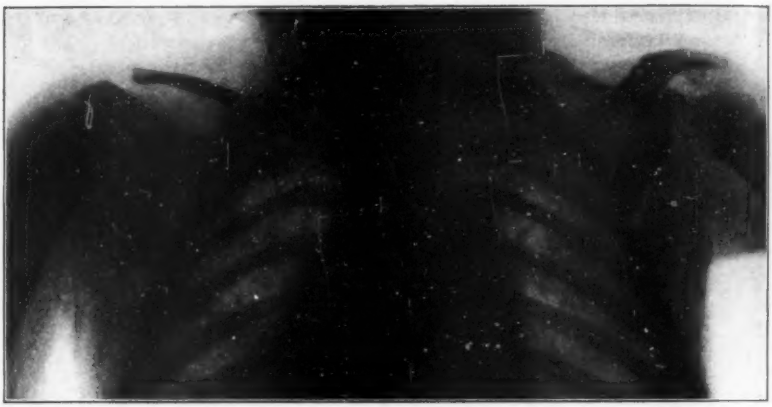
FIG. 6.



Operation was advised, and was done in April, 1901. The joint was exposed by Phelps' incision and the capsule opened. The head of the humerus presented only a very slight degree of atrophy, and the same was true of the glenoid cavity. After breaking up some adhesions the dislocation was readily reduced and the redundant capsule freely resected, after which it was closed with catgut sutures. A plaster dressing was applied, with the elbow held back, which was removed at the end of three weeks.

At the present time the result is most satisfactory. Examination of the child in June, 1902, showed that considerable use of the arm had been gained. He can now feed himself with the right hand and touch his forehead; the hand, however, cannot be placed on the top of the

FIG. 7.



head. Backward movements are improved, although not as perfect as might be desired; but, on the whole, the ultimate result of the operation has been more than satisfactory

A CASE OF MYELOGENOUS LEUKÆMIA, WITH SEVERAL UNUSUAL FEATURES (ABSENCE OF EOSINOPHILIC LEUCOCYTES).

BY CHARLES E. SIMON, M.D.,
OF BALTIMORE, MD.

THE following case of leukæmia, which I have been able to follow for a period of nearly eighteen months and which recently came to a termination, presents a number of interesting features that warrant its publication in some detail.

C. T. F., aged forty-two years; married; printer.

Family History. Mother living; father died of meningitis (cerebral?).

Personal History. The patient has always been in good health and strong, excepting an attack of dysentery which occurred about twelve years ago. This has been followed by several attacks, the last one about eighteen months ago. After the diarrhœa ceased his strength was very slow in returning; he was readily fatigued by any effort, both physical and mental. When I first saw the patient (October 24, 1900) he complained of the passage of mucus in the stools, some pain after eating, general lassitude, and some degree of nervousness. The

appetite was not very good, and the bowels inclined to constipation. There was no nausea or vomiting. The pain occurred not only after meals, but at times also without regard to the taking of food. There was no pain during defecation and no blood in the stools. He had lost about ten to fifteen pounds; his usual weight is 140 to 145 pounds.

Examination at this time revealed the following condition: The patient is a well-built man, about five feet six inches in height, weighing 131 pounds. His color is sallow, but at this time I was not struck by the existence of a special grade of anæmia. The tongue was somewhat pale and moderately furred. Examination of the thorax showed no abnormalities. The abdomen was soft, nowhere painful, and the liver and spleen not palpable. Examination of the urine at this time was negative, and examination of a stool a few days later showed nothing unusual. At that time there was no mucus visible with the naked eye, and no blood. It was partly formed and of a natural color.

The patient was placed on a diet from which butchers' meat and carbohydrates in excess had been excluded, and ordered nux vomica; he was also instructed to use oil injections. On November 24th he reported that his bowels had been normal and regular since he began with the oil injections, three weeks ago. He feels much better in general, and has gotten over his feelings of weakness and inertia practically altogether.

The patient was then not seen until January 4, 1901, when he returned, as he said, to report that he was feeling quite well and had had no further trouble with his bowels. It was then noticed that his color was decidedly below par, and a hæmoglobin estimation showed but 40 per cent. (Fleischl), while the red corpuscles were down to 1,350,000. His leucocytes did not appear to be much increased at that time. A differential count showed about 6 per cent. of neutrophilic myelocytes and no eosinophilic cells or mast cells whatever, so far as I can remember. There was a fair number of normoblasts, and, after prolonged search, a few megaloblasts were also seen; some red cells were undergoing granular degeneration, and a number of polychromatophilic red cells were likewise encountered. There was some poikilocytosis, though not of high grade, and no decided tendency either to oval form or over size.

The patient at that time weighed 131 pounds. His color was not yellowish, but very pale, especially his ears, which appeared almost bloodless. Careful inquiry at this time into any possible causes of his anæmia failed to elicit any information of importance. He had been exposed to lead some years ago, but had never had any symptoms and had not worked in lead for a number of years. Another careful examination of a stool after a purge showed nothing of moment. He denied ever having had syphilis. He has had no hemorrhages, and there were no piles. He also stated that he had never had much color, but that possibly he was paler than usual since the foregoing summer. He stated at this time that his sexual desire was much impaired during the past six months. He was placed on Blaud's pills in increasing doses and the nux vomica continued.

January 22d his hæmoglobin had diminished to 35 per cent., while the myelocytes had increased to 9 per cent. Fowler's solution was then started.

29*th*. No change.

Although the patient was urged to report at regular intervals, he

was not seen again until March 9th. He then stated that he had really been feeling quite well and had noticed no special effect from the arsenic, and had discontinued it, after having taken from three to five drops for a couple of weeks. The hæmoglobin was now 27 per cent., and the myelocytes 12 per cent. The weight was 130 pounds. Examination of the abdomen showed no splenic enlargement. There was no glandular enlargement anywhere, and no tenderness on percussion over the bones. The urine was negative.

After this the patient was not seen until June 3d, when Dr. W. S. Thayer saw him in my absence. At that time the following note was made: Patient is well nourished; color very pale; not yellowish; lips and mucous membranes strikingly pale; tongue reddish in the middle, pale on edges. Thorax symmetrical, costal angle about 90°; resonance clear in front and axillæ; respiration clear. Heart: Point of maximum impulse in the fifth, just inside the nipple line; no enlargement of dulness to the right; first sound accompanied by a blowing, systolic murmur, lost in the mid-axilla; second sound clear. Murmur is feebler at the tricuspid; well marked at the aortic and pulmonic orifices. Abdomen natural; liver just palpable below the costal margin—about a finger's breadth below the costal margin on deep inspiration. Patient has rather a sallow, grayish anæmia.

A fresh specimen showed considerable differences in the size of the corpuscles; a good deal of poikilocytosis, but not as much as one commonly sees in pernicious anæmia; well-marked leucocytosis. The blood record of the dried specimens was unfortunately lost. Color index was not increased. There were slightly over 2,000,000 red cells. There was a distinct polynuclear leucocytosis (?). The patient was ordered Blaud's pills, plenty of milk, and a vacation in the Adirondacks. He returned in August, looking decidedly better, and was ordered to continue Blaud's pills. On October 15th Dr. Thayer saw him once more and noted that the patient was feeling much better and had gone back to his regular business. Red corpuscles then 3,968,000, leucocytes 14,000, and hæmoglobin 40 per cent.

After this I saw the patient again on January 11th, when he returned to see "just where he stood." He looked very pale, but did not complain especially beyond feeling a little fagged and readily becoming short of breath on exertion. The systolic murmur at the apex was then quite distinct, and was heard all over the precordia. The spleen could be felt a little below the costal margin; the liver was not palpable.

Red cells, 1,636,000; leucocytes, 10,200; ratio of whites to reds, 1:162. Hæmoglobin, 35 per cent. A differential count of 591 leucocytes gave the following result (eosinate of methylene blue):

Small mononuclears	11.9 per cent.
Large mononuclears and transition forms	7.9 "
Polymorphonuclear neutrophiles	50.7 "
Eosinophiles	0.0 "
Neutrophilic myelocytes	29.1 "
Mast cells	0.1 "

While counting the leucocytes seven normoblasts were seen and three megaloblasts; it was observed that in many of the normoblasts the nucleus was merely surrounded by a little hood-like appendage of polychromatophilic protoplasm. The nuclei were decidedly pyknotic.

There was a fair grade of granular degeneration, but not so extensive as we commonly see it in cases of well-advanced pernicious anæmia.

The patient was urged to attend to his condition more carefully, to resume his arsenic, and to rest.

On January 15th he saw Dr. Thayer, who then confirmed the condition of the spleen. He notes: the abdomen is natural; the spleen not visible. On deep inspiration, when the ribs are pressed behind, the spleen extends about four centimetres below the costal margin, but it sinks back during inspiration about to a level with this. There is no enlargement of the cervical glands. The point of maximum cardiac impulse is in the fifth space inside the mammillary line, about eight centimetres from the median line. The first sound is a little flapping, with a very soft systolic murmur which is lost as one reaches the anterior axilla, where the sound is decidedly flapping in character. At the base the systolic murmur is barely heard. There is an intense venous hum in the neck over the jugulars, more marked on the right than on the left, and disappearing in the recumbent posture. Recumbent posture brings out the soft systolic murmur at the aortic area and also in the pulmonary, and intensifies that at the apex. Liver not enlarged; flatness not below the costal margin in the mammillary line.

Dried specimens stained with the triple stain show rather marked poikilocytosis; the average size of the corpuscles is apparently normal; a considerable number of nucleated red corpuscles, mostly normoblasts; two very large megaloblasts were seen; one of them showed a nucleus clearly in the process of karyokinesis (aster); another showed two large deeply staining nuclei side by side, evidently having just divided. There were a certain number of nucleated red corpuscles with fragmented nuclei. There was very marked leucocytosis. A differential count of 1000 leucocytes showed:

Small mononuclears	14.3 per cent.
Large mononuclears and transition forms	7.2 "
Polymorphonuclear neutrophiles	47.8 "
Neutrophilic myelocytes	30.3 "
Mast cells	0.2 "
Eosinophiles	0.0 "

Many of the myelocytes were small elements scarcely larger than an ordinary polymorphonuclear leucocyte, although some large typical forms were seen. No eosinophiles were seen in fully an hour and a half's study of two specimens.

January 25th. Condition unchanged. Red cells, 2,080,000; leucocytes, 8950; hæmoglobin, 30 per cent. A differential count of 1000 leucocytes gave the following result (eosinate):

Small mononuclears	10.8 per cent.
Large mononuclears and transition forms	4.9 "
Polymorphonuclear neutrophiles	44.9 "
Neutrophilic myelocytes	39.4 "
Mast cells	0.1 "
Eosinophiles	0.0 "

While counting the 1000 leucocytes, fifteen nucleated red cells were seen, of which three were megaloblasts.

February 8th. The hæmoglobin has fallen to 20 per cent. (Fleischl). Red cells, 1,600,000.

Small mononuclears	7.9 per cent.
Large mononuclears and transition forms	7.0 "
Polymorphonuclear neutrophiles	46.7 "
Neutrophilic myelocytes	37.4 "
Mast cells	0.8 "
Eosinophiles	0.0 "

Granule cells were quite numerous, and polychromatophilia pronounced. Nucleated red cells were mostly of the normoblastic type, but a few megaloblasts were also seen. Most of the nucleated cells were markedly polychromatophilic, and the protoplasm surrounding the nucleus often disintegrating; in many merely showing like a shaggy hood.

The patient does not feel so well, and appears more inclined to give up his work and to rest on his back. He continues on arsenic, but has not gotten beyond five drops. The condition of the spleen remains unchanged. There is no enlargement of the inguinal glands; the liver is not palpable; there is no tenderness over the bones; no hemorrhages of any kind.

24th. The patient has had an attack of diarrhœa lasting several days. The arsenic is reduced from seven to three drops. Hæmoglobin is 28 per cent. (Dare); the leucocytes number 22,600, the highest number yet reached. A differential count of 896 gave the following result (eosinate):

Small mononuclears	9.0 per cent.
Large mononuclears and transition forms	7.1 "
Polymorphonuclear neutrophiles	30.1 "
Neutrophilic myelocytes	53.5 "
Mast cells	0.0 "
Eosinophiles	0.0 "

Megaloblasts were again seen in small numbers. Granular and polychromatophilic degeneration pronounced. The patient has been resting since last note, and realizes that his condition is serious.

An examination of a stool on March 11th disclosed nothing of interest; there were no ova of parasites. Examination of a specimen of urine for the first time shows a very small amount of albumin (serum albumin and serum globulin); there is no Bence Jones albumin. On microscopic examination an occasional hyaline cast is seen. There is no polyuria. Specific gravity, 1016. Sugar absent. Indican not increased.

March 18th. The patient has been on his back and in the open air, on his veranda, most of the time. Hæmoglobin, 34 per cent. (Dare); red cells, 2,842,000 (!); leucocytes, 25,650. A differential count of 581 leucocytes gave the following results (eosinate):

Small mononuclears	5.1 per cent.
Large mononuclears and transition forms	8.2 "
Polymorphonuclear neutrophiles	42.5 "
Neutrophilic myelocytes	43.5 "
Mast cells	0.5 "
Eosinophiles	0.0 "

Granular degeneration was well marked, some of the cells presenting unusually large granules and little, irregular rods. Normoblasts were

common; megaloblasts as in previous examinations. All the nucleated red cells practically were polychromatic, and most of them provided only with a shaggy, narrow zone of degenerating protoplasm.

The patient was told to continue his rest and to be out-of-doors as long as possible and whenever possible. He continues his arsenic.

April 14*th*. He has stopped his arsenic for a few days, as his appetite became impaired, and he had another attack of diarrhœa. He has now been on his back for nearly eight weeks. Condition otherwise unchanged. Hæmoglobin, 42 per cent.; red cells, 2,100,000; leucocytes, 10,500. A differential count gave the following results (eosinate):

Small mononuclears	10.8 per cent.
Large mononuclears and transition forms	8.8 "
Polymorphonuclear neutrophiles	44.4 "
Neutrophilic myelocytes	36.0 "
Mast cells	0.5 "
Eosinophiles	0.0 "

May 14*th*. In order to obtain a more bracing air and to be out-of-doors more, the patient went to Atlantic City. He returns looking much better, sunburned. He feels much better. His spleen is readily to be felt below the costal margin. No glandular enlargement. Liver not palpable. Urine shows a very small amount of albumin; there is no Bence Jones albumin. No pain in the bones, either spontaneous or on percussion. Condition of heart as before. A differential count of 653 leucocytes gave the following results (eosinate):

Small lymphocytes	8.2 per cent.
Large lymphocytes	9.0 "
Large mononuclears (lymphoid cells)	13.5 "
Polymorphonuclear neutrophiles	41.6 "
Neutrophilic myelocytes	27.2 "
Mast cells	1.3 "
Eosinophiles	0.0 "

While counting the 653 white cells only five nucleated red corpuscles were met with; of these two were megaloblasts. The degree of granular degeneration was not so extensive as before, but polychromatophilic degeneration about the same. Some of the lymphoid cells (see below) were exceedingly large; one cell measured 15 x 17.5μ.

The patient then returned to Atlantic City. He was next seen, during my absence, by Dr. Thayer, to whom I am indebted for the following notes also:

June 15*th*. Patient was seen at his house with Dr. Smart. About a week ago he returned home from a trip to Atlantic City, feeling much improved. But about three days ago he began to have headache, fever, and in the mornings noticed a little blood in the mouth. Yesterday the gums became sore and the glands under the jaw began to enlarge.

The patient is in bed, sunburned; vessels on forehead seem unusually full; has a slight puffy look to his eyelids and a slight yellowish tinge to the complexion. The mucous membranes of the tongue are extremely pale. The gums in several places are swollen and black from hemorrhages into the tissue. The pulse is rapid and small; skin hot. The chest is clear in front and in the axillæ. Heart: Loud systolic murmur heard all over the cardiac area. Abdomen natural. The spleen reaches nearly to the umbilicus, nine centimetres below the

costal margin on quiet breathing. The liver is two fingers' breadth below the costal margin in the mammillary line. No tenderness over the long bones. The glands under the jaw are moderately enlarged and slightly tender. Small discrete glands are felt in all parts of the neck and axillæ. Inguinal glands slightly enlarged.

Hæmoglobin, 39 per cent.; red cells, 1,932,000; leucocytes, 116,000 (!). A differential count of 1000 leucocytes showed the following (triple stain):

Small mononuclears	4.18	per cent.
Large mononuclears and transition forms	29.8	"
Polymorphonuclear neutrophiles	17.9	"
Neutrophilic myelocytes	46.9	"
Mast cells	0.6	"
Eosinophiles	0.0	"

There is considerable poikilocytosis; a moderate number of nucleated red corpuscles, much fewer than in the January specimens; most of these were normoblasts, some with fragmenting nuclei. One large nucleated red corpuscle was seen, fully as large as a polymorphonuclear leucocyte, with a large deeply-staining nucleus. Over one-fourth of the leucocytes consist of large mononuclears and transition forms. These are large cells with rather pale nuclei, though in many instances the nucleus takes on a fairly deep color. The protoplasm is sometimes clear and colorless, but is more commonly stained a slightly lilac color. The nuclei are large, round, or bean-shaped, often with sharp, deep, nicks, sometimes dividing the nucleus into several irregular pieces. A considerable number of these cells showed true polymorphous nuclei with homogeneous lilac-staining protoplasm. These nuclei, however, were larger and paler than those of the polymorphonuclear neutrophiles. But one eosinophilic cell was seen on a careful study of two good specimens, and this was found only while studying the specimens with the low power to find nucleated red corpuscles. The myelocytes were, for the most part, very large and characteristic.

The Fowler solution, which the patient has been taking more or less constantly, was omitted, and arsenious acid (one-sixth grain) ordered in pill form, with iron. Mouth-wash of carbolic acid.

13*th*. Seen again with Dr. Smart. The patient has had continuously high fever from 101° to 104° F.; pulse to-day 110 to 130. The enlargement of the glands under the left jaw has increased. The skin is very yellow, and there is a fine petechial eruption on the forehead and face; less over the rest of the trunk and extremities. The patient is very weak, pulse at time of visit 128, small and of low tension. The gums of the lower jaw, about under the right canine tooth, show a wedge-shaped area about one centimetre in extent, which is black and necrotic; a smaller area about a carious bicuspid tooth in the upper jaw is also sloughing. There is a general stomatitis; the mucous membranes are covered in numerous areas by superficial white membranes. The mind is quite clear.

18*th*. The temperature has gradually fallen to normal, and the pulse has diminished in rate, being now from 100 to 110; but the patient has been very weak and has had difficulty in taking his food, partly on account of nausea, partly on account of the soreness of the mouth. The complexion is of a deep, sallow, yellowish color. More purpuric spots have appeared on the face and all over the body. The

spleen reaches to the umbilicus. The glands under the jaw are somewhat less swollen. The areas in the gums, which were previously black, are now suppurating freely, and there is an extensive foul suppurative, in some instances apparently gangrenous, stomatitis in different spots on the gums of each jaw. The patient lies in a dull apathetic condition, and when I came into the room asked me in a whisper to look out for the condition of his nerves, as if he feared that he was becoming delirious. The hæmoglobin was 32 per cent. Absolute counts were not made, but a superficial examination of the blood would suggest that the number of leucocytes had increased.

A differential count of 923 leucocytes which I made from specimens which Dr. Thayer kindly placed at my disposal gave the following results:

Small lymphocytes	0.6 per cent.
Large lymphocytes	0.5 "
Lymphoid cells	54.8 "
Polymorphonuclear neutrophiles	18.5 "
Neutrophilic myelocytes	25.0 "
Mast cells	0.4 "
Eosinophiles	0.0 "

While counting the 923 leucocytes no nucleated red cells were seen, but in otherwise studying the preparation a few were encountered. Granular degeneration was not noticeable at all, and polychromasia but little pronounced. Most remarkable was the large percentage of the "lymphoid" cells.

After Dr. Thayer's last visit the temperature rose again, but did not exceed 101.5° F. The pulse and respiration were about in proportion to the height of the temperature. The patient rapidly lost ground. There was much nausea and occasional vomiting, and on two occasions he complained of pain in the left side. There was some slight bleeding from the gums. Stupor became more and more marked; the pulse feebler and feebler, and death finally occurred in coma on June 22d. An autopsy was unfortunately not obtained.

CONDENSED TABLE OF BLOOD EXAMINATIONS.

Date.	Hb.	Color index	Total No. of red cells.	Total No. of leucocytes.	Lymphocytes.	Large mononuclear elements.	Polymorphonuclear neutrophiles.	Neutrophilic myelocytes.	Eosinophiles.	Mast cells.
1901					Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.
Jan. 4	40	1.5	1,350,000	not increased	.....	.....	.....	6.0	0	0
" 22	35	...	.....	.....	.....	.....	.....	9.0	0	0
" 29	27	...	.....	.....	.....	.....	.....	12.0	0	0
June 3	...	...	2,000,000	increased						
Oct. 15	40	0.5	3,968,000	14,000						
1902										
Jan. 11	35	1.0	1,636,000	10,200	11.9	7.9	50.7	29.1	0	0.1
" 15	...	...	.....	.....	14.3	7.2	47.8	30.3	0	0.2
" 25	30	0.7	2,080,000	8,950	10.8	4.9	44.9	39.4	0	0.1
Feb. 8	20	0.6	1,600,000	.....	7.9	7.0	46.7	37.4	0	0.8
" 24	28	...	.....	22,600	9.0	7.1	30.1	53.5	0	0.0
March 18	34	0.6	2,842,000	25,650	5.1	8.2	42.5	43.5	0	0.5
April 14	42	1.0	2,100,000	10,500	10.8	8.3	44.4	36.0	0	0.5
May 14	...	...	.....	....	8.2	22.5	41.6	27.2	0	1.3
June 15	39	1.0	1,932,000	116,000	4.8	29.8	17.9	46.9	0	0.6
" 18	32	...	.....	very much increased	0.6	55.3	18.5	25.0	0	0.4

To recapitulate in brief we have a patient who becomes markedly anæmic while under general observation, without apparent cause, and who, barring a brief interval during which he seems to have gained some ground, steadily declines in health, and dies at the expiration of seventeen months from the time at which the anæmia was first noted. Subjectively, the patient presents no symptoms until well along in the course of the disease, and then he merely complains of shortness of breath on exertion and a gradually increasing though not very pronounced general weakness. Objectively, we find a very moderate enlargement of the spleen, which, however, only appears after several months, which then slowly increases, but becomes quite extensive toward the end. There is very little glandular enlargement, if any, until quite late in the course of the disease. The oligochromæmia is quite intense from the beginning and out of proportion to the diminution of the red cells. At first there is no hyperleucocytosis; later a moderate increase beyond the physiological maximum occurs, but toward the end this increase reaches very extensive proportions, the ratio of whites to reds falling to 1:16.6. Neutrophilic myelocytes are present from the beginning in notable numbers; they steadily increase until shortly before the end, when they diminish again, but even then do not fall below 25 per cent. There is a corresponding diminution in the number of the polymorphonuclear neutrophiles, and at the same time of the small mononuclear elements. Large mononuclear elements which, through the greater course of the disease were not present in notable numbers, became more numerous, and finally constitute 54.8 per cent. of all leucocytes. Mast cells were at first absent; later they appear, and with some fluctuations they steadily increase until the end. Of eosinophiles only two cells were found in the course of all the examinations, one of which was an eosinophilic myelocyte. Nucleated red cells, both of the normoblastic and megaloblastic variety, were present throughout the course of the disease, but notably much more numerous in the earlier stages. Toward the end but few were seen.

Early in the disease, when the anæmia was first discovered, I regarded the case as one of pernicious anæmia, but the steady increase of the myelocytes, the diminished color index, and the very manifest development of a hyperleucocytosis caused me to abandon this idea, and rather suggested a myelogenous leukæmia as the most likely diagnosis. The case is certainly unusual, however, and does not readily fit the frame of the picture of the disease as modelled by Ehrlich and Lazarus.[1]

The clinical history, to be sure, is not out of the ordinary, and even the slight enlargement of the spleen during the greater period of the

[1] Ehrlich-Lazarus. Leukaemie, etc., Nothnagel's Path. u. Therap, vol. viii., Part I., Heft 3.

disease is not incompatible with the diagnosis. Lazarus states that splenic tumor, though it is usually a dominating symptom, is not of constant occurrence in myelogenous leukæmia, and he cites a case of Litten in which there was only a minimal enlargement. Toward the end, moreover, our patient also presented a well-marked splenic tumor. The remarkable feature of the present case, however, was the condition of the patient's blood, and there are several factors which are here of special interest. First of all, it is noteworthy that until late in the disease there was no grade of hyperleucocytosis that was at all comparable to what is usual in myelogenous leukæmia. In the beginning, indeed, the number of the leucocytes scarcely exceeded the physiological maximum. This factor on first consideration would tend to render the diagnosis of a myelogenous leukæmia doubtful, as a very material increase has usually been regarded as a *sine qua non* in diagnosis. But in view of the large percentage of myelocytes, the clinical history of the disease, and the subsequent development of an extensive polyleucocythæmia, more especially, I scarcely think that this factor alone is capable of influencing our diagnosis. I have looked over the literature in search of still other cases of myelogenous leukæmia in which no very extensive increase of the leucocytes has been observed, and have found two cases which, in this respect at least, can be placed alongside of my own. One is reported by Michaelis,[1] and another by von Noorden.[2] In the first case the total number of leucocytes is given as 16,000, and is said to have remained fairly constant up to the time of death, while the ratio of whites to reds, varied between 1 : 215 and 1 : 150. This case, to be sure, was also not a typical case of myelogenous leukæmia, but rather occupied a position midway between the orthodox lymphatic and myelogenous varieties; nevertheless it was a leukæmia with very manifest involvement of the myeloid tissue (7 per cent. of neutrophilic myelocytes), and the appearance of numerous bone-marrow giant cells in many of the organs. In von Noorden's case, which was a typical instance of myelogenous leukæmia, and is so recognized by Ehrlich, the ratio of whites to reds, did not exceed 1 : 200. Such cases, however, are manifestly rare, and in a survey of the text-book literature on the subject I have not found any additional cases mentioned in which the number of the leucocytes was so low as in the earlier stages of my case. But, after all, there seems to be a growing tendency to attach only secondary importance to the actual number of the leucocytes in the diagnosis of myelogenous leukæmia, as the characteristic feature of the disease is in reality the appearance in the blood of cellular elements which are foreign to it under normal

[1] L. Michaelis. Ueber einen d. Gruppe d. Leukaemie-artigen Erkrankungen zugehörigen Fall, Zeitschr. f. klin. Med., 1902, vol. xlv. p. 87.

[2] Ehrlich and Lazarus, p. 118.

conditions. These elements are the myelocytes, and most important the neutrophilic variety. Upon their presence in considerable numbers, even early in the disease, both Dr. Thayer and I largely based our diagnosis. The occurrence of myelocytes *per se*, of course, would not warrant the diagnosis of a leukæmia, as they may be found in other conditions as well. In the acute infections they may thus appear, but their presence is then probably always associated with a very notable increase of the polymorphonuclear elements, which, indeed, dominate the blood picture. In our case, moreover, there were still other factors denoting serious disease affecting the hæmopoietic organs, which do not constitute a feature of the acute infections. The relative percentage of the myelocytes also increased to such a height as is never observed excepting in myelogenous leukæmia, and their increase in fact was one of the principal factors which caused me to abandon the diagnosis of pernicious anæmia, to which I had at first inclined. Many of the myelocytes were of the smaller variety with trachychromatic nuclei, but there were also present until quite late in the disease notable numbers of the large type with amblychromatic nuclei. Toward the end these latter appeared to be less numerous, and at that time, in fact, the blood picture was controlled to a great extent by the presence of mononuclear elements which were devoid of specific granules and which I have classified in my last differential counts as lymphoid cells. To these I shall return later.

Aside from the comparatively low leucocyte counts during the greater period of the disease, the most remarkable feature of my patient's blood was the practical absence of eosinophiles. I cannot say positively that they were absent early in the disease, as my blood counts from that period were unfortunately lost. My impression, however, is that even at that time they must have been greatly diminished, if not absent; eosinophilic myelocytes at any rate were certainly not observed. But from January, 1902, on I have positive records. I have myself examined many slides of the patient's blood for the sole purpose of discovering eosinophilic cells, and numerous examinations were also made by the gentlemen who were working in my laboratory at the time of the patient's illness, but only one eosinophilic cell was ever found—an eosinophilic myelocyte. In the various examinations which Dr. Thayer made one eosinophile also was only seen. Since the patient's death I have again gone over my preparations with the view of establishing an actual percentage of eosinophiles, but I have had no more success than before, and for practical purposes we can regard the eosinophiles as absent. Granting the correctness of our diagnosis, and I see no reason for abandoning it in view of the marked myelæmia which actually existed, this case represents, so far as I can see, the only case of myelogenous leukæmia with practical absence of eosinophiles that

has been recorded. This is, indeed, most remarkable, in view of Ehrlich's emphatic and frequently repeated statement that the absolute number of the polynuclear eosinophiles is invariably increased in myelogenous leukæmia. This doctrine of Ehrlich has been repeatedly assailed, but hitherto under the mistaken assumption that Ehrlich had reference to the relative number of the eosinophilic cells, when as a matter of fact he has only spoken of an increase in their absolute number. In the present case, however, we may properly say that there were no eosinophiles present in the blood at all. It thus appears that unless our diagnosis of myelogenous leukæmia is abandoned, and, as I have said, I can see no urgent reason for doing so, we must extend our conception of the disease so as to comprise the case under consideration. It might be argued that the absence of the eosinophiles in our case could have been referable to the existence of some septic complication, but, barring the terminal gingivitis, there was no clinical evidence whatever of any septic process at any time which was borne out, moreover, by the non-existence of a polynuclear neutrophilic hyperleucocytosis.

To illustrate the diagnostic value of an absolute increase of the eosinophilic cells in myelogenous leukæmia Ehrlich cites a case of bone-marow carcinomatosis, reported by Epstein,[1] in which a leukæmoid condition of the blood was noted, and "in which the absence of eosinophilic cells excluded the existenceof true leukæmia." In this case a notable increase of the leucocytes was noted, the ratio of whites to reds varying between 1 : 25 to 1 : 40; numerous nucleated red cells, both of the normoblastic and megaloblastic type were seen, and in addition there were present a considerable number of neutrophilic myelocytes. Of eosinophiles only two cells were found in all the preparations that were made in the course of fifteen days. In my own case there could be no question of the non-existence of malignant disease in the sense of a carcinomatous involvement of the bone-marrow. The clinical history and the course of the disease are entirely opposed to such an assumption, and suffice to exclude their existence, even though an autopsy was not made.

A further consideration also, which might suggest itself as a possible explanation of the case—*i. e.*, the existence of multiple myeloma of the bone-marrow, can be ruled out. That multiple myeloma may terminate under the picture of a leukæmia is possible, as shown by the case of Askanazy.[2] The absence of Bence Jones albumin, however, and the

[1] J. Epstein. Blutbefunde b. metastatischer Carcinose d. Knochenmarks, Zeitsch. f. klin. Med., 1896, vol. xxx. p. 121.

[2] This case, it is true, is usually cited to illustrate that the Bence Jones albumin is not absolutely pathognomonic of myeloma; but I must confess that the extensive rarefaction of the bone substance is, nevertheless, strongly suggestive of the disease.—S. Askanazy, Deutsch. Arch. f. klin. Med., 1900, p. 34.

fact that the patient at no time complained of pain in the bones, either spontaneously or on percussion, conjointly tend to throw out such a possibility in our case.

It seems to me, after carefully weighing all the possible explanations which could be offered of a blood find as we see it in our case on the basis of something else than a myelogenous leukæmia, that we must still adhere to our diagnosis, or we must admit that a non-leukæmic condition may exist in which neutrophilic myelocytes can occur in the blood to the extent of 46.9 per cent., corresponding to an absolute number of 54,404 (!), and in which the total number of leucocytes may reach 116,000 pro cbmm., coincidently with the existence of a splenic tumor reaching nearly to the umbilicus. A concurrence of these three factors has, so far as I know, not been observed outside of myelogenous leukæmia, and we are thus forced to the conclusion that, after all, cases of the disease may occur in which the eosinophiles are neither relatively nor absolutely increased. I have looked over the literature so far as it was accessible to me in the attempt to find a parallel case to my own, but have not been successful. I have, however, met with at least one instance of leukæmia with undoubted involvement of the bone-marrow, in which a total increase of the eosinophiles likewise did not exist, and which in a measure may be regarded as illustrating an intermediary stage of the disease between the typical myelogenous variety with absolute eosinophilia, and my own case. This case is that of Michaelis,[1] already referred to. With a leucocytosis of 16,000, the percentage of eosinophiles was only 0.4, thus corresponding to a total of 64 cells, as compared with a maximum normal of 250, as given by Zappert.[2]

Equally striking at first as the absence of eosinophiles in my case was the low percentage of the mast cells, and, early in the disease also, their low absolute numbers. I dwell on this in view of Ehrlich's statement that the mast cells are absolutely increased in all cases of myelogenous leukæmia, and that their presence in increased numbers is even more important from the standpoint of differential diagnosis than that of the eosinophiles.

But, while their number at first was not only relatively but also absolutely low, a definite increase occurred later in the disease. Still, as late as January 11th the total number was only 10 per cbmm., and on January 25th even less—*i. e.*, 8.9 per cbmm. A relative increase then occurred to 0.8 per cent., which was followed by a decrease to zero on February 24th. By March 18th, however, they had increased to 0.5 per cent., corresponding to a total of 128, and on May 14th, 1.3 per cent. were counted. The last absolute count was made on June

[1] Michaelis. Loc cit.

[2] J. Zappert. Ueber d. Vorkomen d. eosinophilen Zellen im anaemischen Blut. Zeitsch. f. klin. Med., 1893, vol. xxiii.

15th, when the percentage was only 0.6, but the total number 696! We thus see that at a time when the disease was fully developed there existed a very marked increase of the mast cells, which fact still further strengthens our assumption that the case was in reality one of myelogenous leukæmia.

In conclusion, I wish to refer to the decided increase of the mononuclear elements devoid of granules which occurred toward the end of the disease, when fully 55 per cent. of all leucocytes belonged to this category. Of these, moreover, 54.8 per cent. were of a type which manifestly is distinctly different from the large mononuclear elements of normal blood. This difference, to be sure, is not so apparent in preparations that have been stained with Ehrlich's triple stain, but it becomes very manifest in specimens that have been stained with the eosinate of methylene blue which, after all, is much better adapted to the study of the mononuclear elements. The exact position which these cells occupy among the elements of the blood is still a matter of dispute. They are certainly not identical with the common, small lymphocytes, as they lack the narrow rim of deeply-staining basophilic protoplasm, the sharply defined nucleus, and as they are much larger in size. In 1895, Fränkel[1] described a type of cell as occurring in acute (lymphatic) leukæmia, which corresponds to our form more closely. These cells are large and provided with a large, feebly-staining, round or karyolobic nucleus which is surrounded by a narrow zone of non-granular basophilic protoplasm. He regarded these cells as large lymphocytes and as derivatives of the common smaller variety. Similar cells have been observed in the germinal centres of lymph glands, and were termed by Benda[2] lymphogonia, while corresponding cells which he found in the bone-marrow were designated as myelogonia. These latter in turn are possibly identical with Troje's[3] marrow cells, and Grawitz's[4] "immature" cells, of which he supposed that under certain conditions they might take up granules and thus become myelocytes. The normal occurrence of non-granular mononuclear leucocytes in the bone-marrow, which was still doubted, has now been definitely established through the researches of Pappenheim,[5] Rubinstein,[6] and others, and it is quite likely that all these various types are in reality identical and to be distinguished from the common lymphocytes and large mononuclear leucocytes of the blood. Nägeli,[7] also,

[1] A. Fränkel. Ueber akute Leukaemie, Deutsch. med. Woch., 1895, Nos. 39–45.
[2] Benda. Anat. Mittheil. über acute Leukaemie. Verhandl. d. 15 Cong. f. inn. Med., 1899.
[3] Troje. Ueber Leukaemie u. Pseudoleukaemie. Berl. klin. Woch., 1892, No. 12.
[4] Grawitz. Klinische Pathol. d. Blutes, 1896.
[5] Pappenheim. Ueber Lymphaemie ohne Lymphdrüsenschwellung. Zeitsch. f. klin. Med., 1900, vol. xxxix. p. 171.
[6] Rubinstein. Zeitsch. f. klin. Med., 1901, vol. xliii. p. 161.
[7] Nägeli. Ueber rothes Knochenmark u. Myeloblasten. Deutsch. med. Woch., 1900, No. 18.

does not regard the non-granular cells of the normal bone-marrow as a species of lymphocytes, but as specific bone-marrow cells, which he terms myeloblasts, and, like Pappenheim, regards as antecedents of Ehrlich's myelocytes. As he has pointed out, these cells are found in the blood in every case of myelogenous leukæmia, and may in the later stages, as in our case, represent the greater proportion of all the leucocytes. Michaelis and Wolff[1] term these cells lymphoid cells, in contradistinction to the lymphocytes of the blood; they wish to convey the idea that the bone-marrow lymphocyte is still capable of a relative differentiation, while this is no longer possible in the case of the common lymphocyte of the blood. Pappenheim regards these cells, which correspond to his large lymphocytes, as the mother cells of the small lymphocytes, of the red cells and of the myelocytes, and, as I have said, it seems well established that these cells are normally found not only in lymph glands and other organs of the body, but also in the bone-marrow. With these cells, I think, the "large mononuclear" elements in my case are identical. As I have said, they differ markedly from the common lymphocyte, and they certainly do not resemble the ordinary large mononuclear elements of the normal blood. It might, of course, be suggested that these large mononuclear elements, which, with Wolff and Michaelis, I shall term lymphoid cells, represent myelocytes that have lost their neutrophilic granulation. That such an occurrence may be possible is undoubted. Zappert,[2] Ehrlich-Blachstein,[3] and Arneth[4] have described such cases, and Ehrlich,[5] himself, reports on the absence of neutrophilic granules in the polynuclear leucocytes in a case of post-hemorrhagic anæmia. Everyone, moreover, who has busied himself to any degree with the study of the blood in pathological conditions will have observed that under certain conditions the amount of neutrophilic material is very much diminished. Sometimes, it is true, this is only apparent, and it may be possible by a suitable modification of technique to bring out the granules even in cases in which they appear to be absent. An explanation of such anomalous conditions cannot be given; but, as I have said, everyone who has busied himself to any degree with such matters is perfectly familiar with their occurrence. In my case, however, this explanation certainly does not hold good, even though a marked diminution of the neutrophilic material had also occurred toward the end of life. That they may be related to the myelocytes I do not wish to

[1] Michaelis und Wolff. Die Lymphocyten. Deutsch. med. Woch., 1901, p. 651.
[2] Cited by Ehrlich-Lazarus. Die Anaemie Loc. cit., p. 126.
[3] Ehrlich-Blachstein. Ibid., p. 126
[4] Arneth. Haematologische Befunde zu Leube: Ueber einen Fall von rapid verlaufender schwerer Anaemie mit gleichzeitiger leukaemischer Beschaffenheit d. Blutes. Deutsche Arch. f. klin. Med., vol. lxix., Heft 3 and 4.
[5] Ehrlich. Die Anaemie, p. 89.

deny, for we meet with cells, on the one hand, in which the protoplasm begins to show a decided granular appearance, the granules staining with basic dyes, and, on the other hand, we see cells of this second type in which neutrophilic granules are just beginning to appear and in which the protoplasm is scarcely basophilic at all, but is beginning to show distinct oxyphilic tendencies.

In much of the past work on the morphology of the blood in myelogenous leukæmia sufficient attention has not been directed to the mononuclear non-granular elements which appear in the circulating blood, and most observers have contented themselves with describing such elements as large mononuclear leucocytes. So long as the tendency exists to employ only the "allein-selig-machende" triple stain of Ehrlich, as Pappenheim quaintly terms it, but little progress is to be anticipated, from the clinical side, in the attempt to clear up the mooted question of the classification of the leukæmias. Some work, however, has been done to break through the rigid barriers which Ehrlich and his school have erected between the lymphatic and the myelogenous varieties, and, so far as the blood picture can serve as a basis of classification, there seems to be good ground for the recognition of three forms of leukæmia, as Reed[1] suggests, which are all due to myelogenous changes. These forms may be known as the myelogenous, the lymphoid and mixed-cell varieties, all of which in turn may be either acute or chronic, the general tendency of the first being toward chronicity and of the second toward an acute course. It appears, moreover, that cases of the first order may pass over into the second type, though the reverse has not been definitely proven. Cases representing the mixed-celled variety will probably become more frequent when clinicians will hav learned to depend not only on the triple stain, but to carry their differentiation beyond its limits. Cases of this order have been reported by Michaelis[2] and Wolff,[3] and possibly the cases of Bloch and Hirschfeld,[4] and that of Arneth[5] also belong to this category.

To attempt an explanation of the absence of the eosinophiles in the present case seems scarcely practical, especially as no autopsy was had, and we are unable to affirm that the production of eosinophilic cells was actually arrested. That such was the case, however, seems a fairly logical inference, in view of the fact that eosinophilic myelocytes also

[1] D. M. Reed. Acute Lymphatic Leukæmia without Enlargement of the Lymph Glands, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1902, vol. CXXIV. p. 658.

[2] Loc. cit.

[3] A. Wolff. Ueber d. Bedentung d. Lymphoidzelle b. d. normalen Blutbildung u. b. d. Leukæmie, Zeitsch. f. klin. Med., 1902, vol. xliv. p. 385.

[4] Bloch and Hirschfeld. Zur Kenntniss d. Veränderungen am Centralnerven-system b. d. Leukaemie, Zeitsch. f. klin. Med., 1900, vol. XXXIX. p. 32.

[5] J. Arneth. Loc. cit.

did not appear. The absence of the polynuclear variety might be explained on the basis of negatively chemotactic influences being at work (contrary to the usual, to be sure), in which case their production need not have been arrested. But this explanation can hardly be applicable in the case of the eosinophilic myelocytes, if, with Ehrlich, we regard all mononuclear cells as not subject to the law of chemotaxis.

THE DERMATOSES OCCURRING IN EXOPHTHALMIC GOITRE.*

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and
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The dermatoses occurring in the group of affections commonly described in this day as belonging to "inner medicine" do not always sustain definite relations to what may be termed the essential morbid process. Some cutaneous manifestations, as, for example, in the exanthematous fevers, are more or less constant syndromes of the systemic condition. Others, as the xanthoma of glycosuria, are the rare and exceptional concomitants of the general disease.

It is the last-named group of disorders the etiological relations of which are to be viewed with caution if not suspicion. Given such a malady as Asiatic cholera, in which by far the larger number of victims exhibit no changes in the skin, the inference is natural that in the exceptional cases the intervention of some novel and accidental agency has wrought the unusual result.

These considerations have force in relation to exophthalmic goitre, known also as Basedow's or Graves' disease, an affection for the most part unaccompanied by skin symptoms, and yet one which at times exhibits in the course of its evolution changes in the integument of the highest importance. For example, under the title "Cutaneous Affections Occurring in the Course of Graves' Disease," S. E. Dore[1] in 1900, published a valuable report of leucodermatous and other changes in the skin occurring in coexistence with exophthalmic goitre; the author also presenting a survey of the literature of the subject at the date of his paper.

As to the essential or accidental connection of these cutaneous syndromes with the general pathological state, a due reserve can be admitted by recognizing the fact that with respect to the other ailments of the

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general economy the tegumentary symptoms may be somewhat loosely classified as follows:

In a first group may be named the dermatoses which represent a purely accidental concurrence with symptoms indicative of the general ill health of the subject of the disease. Thus, for example, patches of tinea versicolor may be seen on the surface of the chest of a patient suffering from pulmonary tuberculosis.

In a second group may be included those changes in the skin which are more or less *distantly* related to the essential morbid process. The cutaneous symptoms may be directly due to a non-cutaneous manifestation, which in turn is dependent upon some factor more nearly related to the causal element in the general disease. Thus the sudamina of typhoid fever are the remote outcome of the fundamental morbid process—*i. e.*, infection with the bacillus of typhoid; for several intermediary conditions are traceable, each one of which is more or less essential to that which follows it. A concise expression of the evolution would be as follows: typhoid infection, impression on nerve centres, vasomotor instability, hyperidrosis, sudamina.

In a third group may be recognized those morbid symptoms in the skin which are *intimately* related to the systemic disease. In illustration of the disorders here classed may be cited the exanthemata and the purpuras of septic infection, in all of which the result is produced by the direct action of the specific organism or its toxines on the structures composing the skin.

To one or another of these categories may be assigned, together with the cases the brief records of which are appended, the histories in medical literature of similar import.

CASE I. *Exophthalmic Goitre and Hidrocystoma.* Mrs. L. D., thirty-nine years of age, married eleven years and mother of two living and healthy children, had had three miscarriages. She weighed 156 pounds and had previously enjoyed good health. She consulted one of us first in 1884, for relief of a vulvar ulcer which was believed by herself and her husband to have been the result of the employment of a soiled vaginal speculum in the hands of a gynecologist. This lesion healed under local treatment and no consequences were noted.

In the year 1875, this patient consulted us again for relief of a cutaneous pruritus which yielded promptly to simple treatment.

On the 5th of May, 1902, she again sought relief, and on this occasion complained of certain facial lesions the unsightliness of which distressed her. She was now fifty-seven years of age, and had been living in a home surrounded by all the luxuries which large wealth commands. Some weeks before the consultation, she had suffered from an enervating fever, to the weakness resulting from which she referred her trouble. During the preceding month, she had not been living in a moist atmosphere; and had been, on the advice of her family physician, resting as quietly as possible during the most of the day in a reclining chair.

When examined she was found to have an enlargement of the thyroid gland which had attained the size of a small orange. There was marked exophthalmos, classical tremor, great weakness, and some inappetence. Her pulse was 110 to the minute, soft, compressible, and full; there was no murmur either cardiac or vascular. Her color was a dull gray, her mind active, her intelligence (always of a high order) unimpaired. On the slightest exertion she became much prostrated.

The skin of her face was continually moistened with sweat, and the seat of a score or more of vesicles chiefly clustering over the brow, nose, cheeks, and chin. These lesions were elevated, flattened to obtuseness, pea-sized, tense, very well defined, discrete, unaccompanied by signs of inflammation, and occurring in no other region than the face. When punctured, they gave exit to a clear fluid having the color of sweat. When unruptured, some of the larger lesions suggested boiled sago-grains; a few had a dull opalescent hue, others were very slightly empurpled; at a distance, the color was almost that of lead. The relics of a few desiccated lesions, shreds of torn blebs and very ill-defined mottlings of the surface, could be detected.

The lesions, single and in totality, were identical with the symptoms of hidrocystoma ably studied and described by Robinson. We have had an interesting group of cases with exactly similar cutaneous lesions upon the face, in laundresses applying for relief at the clinic, many of whom had been sweating when enveloped in the moist atmosphere surrounding the laundry-tub. The social position of this patient forbade a biopsy of the elements of the eruption.

CASE II. *Exophthalmic Goitre and Telangiectases.* Miss N. M., aged twenty-four years; family history good; had bronchopneumonia at two years; scarlet fever at eleven, with no untoward sequelæ; diphtheria at fourteen, and measles at twenty-one. Menstruation began at thirteen, and has been practically normal except for occasional dysmenorrhœa. She gives no history of pelvic trouble.

The patient had goitre at twelve years, after a severe sore throat; and the gland has remained of about the same size since the beginning of the disease, increasing in volume slightly during "colds." She taught school from seventeen to twenty-four years of age, and does not think she was especially nervous during this time as the result of the strain. About two and a half years ago she was greatly worried over the sickness of a brother ("blood poisoning"). There is no history of alcoholism.

Two years ago the patient noticed a marked redness of the skin over the right frontal eminence; this gradually spread over the forehead. At this time she began to have cardiac palpitation on exertion. There were no other subjective symptoms except weakness in the legs. She said she felt "as though her knees would give out under her."

On examination, she is seen to be poorly nourished, of sickly appearance, and of slender build. Her weight is 112 pounds. The forehead shows a diffuse redness extending to the roots of the hair. On close inspection a fine network of vessels is visible throughout the area, at some points more numerous than at others. Pressure under a glass shows new vessel-formation, with small scattered areas of brown pigment deposits. The redness extends over the cheeks and angles of the jaws to the neck, especially on the left side, where it appears as a tongue-like prolongation over the enlarged left lobe of the thyroid. Part of the red-

ness disappears if the patient remains perfectly quiet for a brief time. New vessels, however, are present over the frontal eminences, the prominences of the cheeks, and over the lobe of the thyroid. The eyes show normal reflexes. Von Graefe's, Stelwagon's, and Möbius' signs are absent. There is a very slight exophthalmos. Circumference of neck measures 29½ cm. Both lobes and the isthmus of the thyroid are moderately enlarged, the left showing greatest change; the gland is soft and not sensitive. The lungs are normal; the heart is normal in size; there are no murmurs; the cardiac pulse is 130 per minute (while the patient is quietly resting), regular and forcible; a murmur is present over the right side of the neck; there is no unusual cervical pulsation. The abdomen is normal; the pelvic organs were not examined. There is no œdema. There is a well-marked tremor in the outstretched hands. All the reflexes are greatly exaggerated. The urine is negative. There are no red or brown patches on body; the skin is moist and irritable.

CASE III. *Cutaneous Pruritus in Exophthalmic Goitre.*—Mrs. J. C., aged forty-two years. Her family history is good; her personal history satisfactory until recent years. Goitre has been present twelve years. Five years ago her health began to fail; there was great palpitation and dyspnœa, with general body weakness. Three years ago cutaneous symptoms began; the skin became irritable; itching at times was intolerable, and the patient constantly excoriated herself in efforts to relieve the pruritic symptoms. Examination showed both lobes of the thyroid enlarged and soft; the heart was normal in size; no murmurs; pulse, 120 to 140, regular; exophthalmos, tremor; urine negative. The skin of the face and of much of the body was reddened, and presented many small, scattered, and torn papules.

CASE IV. *Cutaneous Pruritus and Angioneurotic Œdema in Exophthalmic Goitre.*—Mrs. A. C. J., forty-nine years of age, a widow and mother of two healthy children, had been under the care of a distinguished member of the profession for sixteen years. She had passed the climacteric at forty-six. The full history of the exophthalmic goitre from which she suffered for a large part of this time appears in the records made by her physician. He consulted one of us on February 27, 1899, in consequence of a complicating cutaneous disorder.

The patient was found in bed, pallid in color, with a goitrous enlargement of the size of a large apple, exhibiting marked exophthalmos, having an exceedingly rapid, weak, soft pulse, and showing distinct tremor. Some few weeks before, tubercle bacilli had been recognized in the sputum. She had a slight bronchial cough and dulness on percussion at the pulmonary apices; the skin was for the most part dry. Her treatment for some weeks before had been by internal administration of strophanthus, pilocarpine, and strychnine; with absolute rest and a diet strictly limited to milk and the cereal known in this country as "popcorn." It was a question whether this last had in any way contributed to the cutaneous symptoms, but inasmuch as the latter persisted for some time after the withdrawal of this cereal from the dietary, a causal relation between the two may be doubted.

When examined, the skin was found to be the seat of excessive itching and burning, decidedly most annoying over the lower limbs and the hips, preventing sleep at night and greatly disturbing the digestive processes. In many places the surface was excoriated in attempts to relieve the pruritus by scratching and rubbing. Giant wheals both actively

developed and relics of a former activity in the shape of vivid and dull reddish macules were evident here and there over the surface, especially upon the hips. Complaint was made that in all positions in the bed the skin of these parts gave the patient much distress.

Elsewhere over the body, in trifling measure upon the face and neck, there were pruritic symptoms, evanescent rosy blotches and ill-developed wheals.

By the end of the following month the patient was relieved of the local symptoms by employment of the simpler methods of treatment, including the protection of the surface by the Pick dressing. At the present date the patient is living and has survived a fracture occurring as an accident when ascending the stairs. Her improvement in the diminution in the size of the goitre and the exophthalmic symptoms are unquestionably due to highly scientific management by her physician who has been from the first in charge of her case.

Having in view the instances herein reported and surveying the literature devoted to the special facts which they illustrate, it is clear that important lesions of the skin, some involving serious structural change in the corium and subcutaneous tissue, may coexist with exophthalmic goitre. About one hundred and eleven reports have been made of cases of this character, the list including, first, about forty-nine cases of hyperidrosis; next, each in equal frequency, fifteen of pigmentary changes and myxœdema; about fourteen cases of simple œdema of the skin; five cases of scleroderma, most of them generalized, a small portion representing the circumscribed form; then alopecia, often generalized, and vitiligo; lastly, one or two instances each of telangiectasis, purpura, urticaria, erythema, and one only (that herein reported) of hidrocystoma. Among the accidents of the same morbid process, most of them evidently rare, are hemorrhage from the skin, bronzing of the integument, eczematous and erysipelatous accidents, and localized anæsthesia.

The affections thus catalogued can for the most part be readily assigned to one of the three groups described in the introductory paragraphs of this paper. Thus, for example, it is safe to assume that some of the cases recorded as eczematous, urticarial, erythematous, etc., were either accidental concurrences in the general disorder or were remote reflex disturbances due to irritation of the nervous centres. Again, the marked frequency of hyperidrosis in the list of cutaneous symptoms points unerringly to the vascular disturbance which is so fixed an element in the nosology of exophthalmic goitre, and which it is barely possible may be in turn responsible for the frequency of pigmentation after the existence of the malady for a long period. The intimate relationship existing when such disorders as scleroderma and myxœdema accompany or, as may be the issue, succeed the common signs of Basedow's disease is obvious.

With reference to the patients whose cases are described above, Cases III. and IV. may be referred to the first or second group defined herein,

that in which the cutaneous symptoms are either accidents of the general process, or possible surface indications of the mischief beneath the surface.

With Cases I. and II. there is a marked departure from the limits established for the first group. In a single instance (that of Case I.) the exanthem may be regarded as distinctly though remotely the result of one of the prime symptoms of the general disease. In the other (Case II.) there is a new formation of vessels apparently as the immediate result of the evolution of the malady.

Respecting the first case, that of hidrocystoma complicating exophthalmic goitre, a careful survey of literature has failed to discover any other case. Hyperidrosis, however, a condition in close causal relation to hidrocystoma, as already shown, has been frequently observed. So commonly, in fact, does sweating occur, that it may almost be expected as a symptom in Graves' disease; one of the manifestations of the profound vasomotor instability found in that malady. Dreschfield[2] observed profuse sweating in forty cases, occurring by day as well as by night, most marked in those presenting the most serious symptoms of the general disease. Watson-Williams[3] records a case in which the hyperidrosis affected principally the right side. It is interesting to note also that in this patient von Graefe's sign, dilatation of pupil and enlargement of the thyroid were most pronounced on the right side. Excitement would be followed by profuse sweating of the right leg below the knee. Hector Mackenzie[4] comments on the frequency of hyperidrosis, especially of the palms, and reports several cases. Others have made similar observations. Occasionally, where certain complications have existed, hyperidrosis has not occurred and the skin has been found to be dry.

A special interest, from the point of view of the dermatologist, attaches to the case of hidrocystoma here reported because of the conditions in which the vesicles formed. Robinson has called attention to the circumstance, amply corroborated in our clinical experience, that the special factors of the disease are, first, profuse sweating; second, environment in a moist atmosphere, such as that in which most laundresses labor. With these favoring conditions, it is found that the subjects of the disorder are mostly women and these in middle life or more advanced years, doing work in the summer months. Robinson states, however, that he has observed the disease also in cooks, and indeed in persons who have neither been cooking nor washing. Once only the symptoms occurred in a man twenty-eight years of age, and then upon one side of the nose only. The observation here recorded is of special interest as showing that hidrocystoma may develop in classical symptoms upon the face of a woman in nowise exposed to a moist atmosphere, and doing no work of the kind middle-aged women often

perform. Briefly, it is shown that cardiac and vasomotor disturbances in exophthalmic goitre are capable of inducing the characteristic lesions of the disease. The pathology of the lesions and their relation to the excretory duct of the sweat-gland at some point in the corium has been thoroughly established by Robinson's demonstrations.

With reference to the second case herein reported, it may be said that hyperæmia of the skin is of common occurrence in Graves' disease, as can readily be explained by the irritability of the vasomotors so constantly present. The intercurrence of telangiectases of the skin, however, is very rare. The writers have been able to find but one reported instance. Létienne and Arnal[5] record the case of a woman (Graves' disease) who presented multiple telangiectasic areas over the entire body. The patient was twenty-seven years old, with a family history showing a decided nervous taint. Her personal history was also bad—hysterical crisis at twelve; rheumatism at fifteen; menstrual and digestive derangements. At twenty-six she noticed a small red spot over the sternum; similar macules appeared elsewhere, and one year later examination disclosed the following: round and oval, scarlet to dark red spots, of variable size (not exceeding the diameter of a 50-centime piece), disseminated without order over the entire body, the shoulders and neck excepted. The spots show a dark centre surrounded by a fine network of vessels with arborizations, gradually losing themselves in the surrounding skin; they disappear on pressure; there is no desquamation; two larger areas are present above the malleoli, painful on pressure; no spots on the mucous membrane. The right lobe of the thyroid is hypertrophied. The pulse is regular, 105; no exophthalmos; marked tremor, and great nervousness.

After a period of treatment the patient seemed to improve, though new spots had appeared and none of the old had disappeared. In this case there was a possible etiological factor in alcoholism, of which the patient gave an obscure history. The reporters of the case, however, think the condition to be one of nervous origin.

Although Osler[6] speaks of pruritus as an occasional symptom in Graves' disease, and reports a case in which it constituted a severe and persistent complication, medical literature is singularly devoid of recorded instances in which this cutaneous symptom was prominent.

Greater interest attaches to the subject of œdema in its various forms as associated with exophthalmic goitre. Numerous cases are reported, and the discussion, which is always full, leads by natural and logical sequence to a consideration of myxœdema and scleroderma as related to Graves' disease. Some degree of œdema is present in a large proportion of all cases. It varies in its nature and location. It may be persistent or fleeting; pitting or non-pitting; symmetrical or non-symmetrical; with and without albuminuria. The hands, eyelids, face and

neck, ankles and legs are common sites. Maude[7] has divided the œdema of Graves' disease into three classes: (*a*) from cardiac insufficiency, generally in severe cases; the œdema may appear suddenly and become general; (*b*) of nervous origin; slight swelling of instep and lower legs, without cardiac insufficiency and albuminuria; (*c*) transitory œdema; irregular, unsymmetrical, lasting but a few hours; the arms, hands, neck, and face are usually selected. This class suggests a type of œdema analogous to or identical with that found in giant urticaria; which skin lesion is mentioned by Möbius[8] as occurring in Graves' disease. Maude's classification would seem to be somewhat deficient, as in it no place is found for œdema of renal origin nor for the brawny infiltration (mucoid) which is present when myxœdema is a complication. Hector Mackenzie[9] writes that it is common to find œdema of dependent parts in debilitated subjects of Graves' disease from gravity and an enfeebled heart action, and quotes Basedow as having seen in emaciated patients swelling of the joints and tissues of the abdomen, as well as non-pitting œdema of the legs. He reports seven cases of œdema of the eyelids, in three of which the condition persisted after recovery; two of œdema of the legs, one of which showed persistent albuminuria after disappearance of the swelling; and two cases of persistent, probably mucoid, infiltration of the connective tissue of legs, suggesting myxœdema. Vigouroux[10] has expressed the opinion that the swelling of the eyelids is not always true œdema, but rather a condition due to paresis of the orbicularis muscle. Dreschfield[2] noted transitory œdema in several of his cases, and in Watson-Williams'[3] case œdema of the legs was the first symptom noted.

The relation of Graves' disease to myxœdema is one of exceeding interest, and inasmuch as the condition of the skin and subcutaneous tissues plays an important role in the diagnosis of the latter, a consideration of the relation between the two diseases comes properly within the scope of this paper. A number of cases have been observed in which exophthalmic goitre has been followed gradually by myxœdema, with all the cutaneous changes which attend that disease. Kowalewski[11] was among the first to report an instance; an epileptic, with well-marked symptoms of Graves' disease, showed, after a paroxysm, swelling of the feet, legs, and face (character of swelling not given). Later mental hebetude developed. He considered myxœdema as an expression of a severe type of Graves' disease. Sollier[12] reports a rather peculiar case in which the myxœdematous (?) symptoms developed first. The patient suffered with pains in the hand. These became swollen, the swelling gradually extending over the entire body. Later the symptoms of Graves' disease came on. When seen by Sollier there was swelling of the entire body, *atrophy* of the thyroid, nervous irritability, exophthalmos, tachycardia, tremor, pigment flecks over body. Under electrical and

hydrotherapeutic treatment all symptoms of myxœdema and nearly all of Graves' disease disappeared. One is not fully convinced that in this case myxœdema was present. In von Jaksch's[13] case typical symptoms of Graves' disease were present; the patient also showed a non-inflammatory, non-pitting swelling of both legs, which gave the impression that some substance more resistant than water was deposited in the subcutaneous tissues, suggesting strongly myxœdema. Williams' case[14] was that of a woman of thirty with Graves' disease, treated with arsenic and change of climate, recovery following. Five years later she became languid; the face, arms, and hands were puffy; there was no albuminuria. Myxœdema was diagnosticated, and recovery followed the use of iron and arsenic. The same year Joffroy and Achard[15] published a case of a woman of twenty-three who presented at first the picture of Graves' disease; later, the goitre and exophthalmos disappeared; she became very weak; œdema of the feet, legs, body, and face developed; there was great mental apathy; death followed, and the autopsy revealed hyperplasia of the connective tissue of the thyroid, with disappearance of parenchyma. Putnam[16] reports a case in which the existence of Graves' disease is somewhat uncertain. A woman of fifty-five years, in whose family myxœdema had occurred twice, developed typical myxœdema, with usual skin changes. This, however, was preceded by two symptoms of Graves' disease, struma and tachycardia. Under thyroid treatment recovery ensued. Four cases are reported by Baldwin:[17] (1) A boy of ten years, sluggish, overgrown, mentally dull; skin dry, harsh, inelastic, and puffy; at six years he had heart trouble, pronounced at the time to be Graves' disease; recovery occurred under thyroid treatment. (2) A girl of fourteen years with typical Graves' disease; six years later a typical myxœdema; improvement under thyroid exhibition. (3) A girl of fifteen years with tachycardia, exophthalmos, tremor, goitre; after six years; mental hebetude, intolerance of cold, poor circulation; skin dry, harsh, inactive; cured with thyroid extract. (4) Woman of forty-four years; nervous history; Graves' disease for four years; later, mental hebetude, intolerance of cold, melancholia; skin harsh and dry, face swollen; cured with thyroid extract.

Loew[18] considers the œdema of nervous origin to be myxœdematous or premonitory of myxœdema. He reports two cases: (1) A woman of twenty-three years, with typical symptoms of exophthalmic goitre; in addition, pigment spots everywhere present, with patches of vitiligo at elbows and knees; the lower part of the legs swollen; skin hard, tight; very slight pitting; the dorsum of the feet not affected. (2) A woman aged twenty-four years, with Graves' disease; the lower limbs from middle of thighs to dorsum of foot swollen, hard, inelastic, non-pitting. A case of Gautier's[19] is reported briefly. In 1894, Graves' disease; im-

provement; in 1895, recrudescence; improvement; in 1898, myxœdema; hard, fibrous thyroid; improvement under thyroid treatment.

Pasteur[20] reports the case of a woman of sixty-five years who developed Graves' disease twenty years before (1878). In 1886 she presented typical symptoms; under observation the enlarged thyroid became atrophic (effect on pulse rate not reported); in 1893 the patient had permanent bradycardia (30–55), cardiac dilatation, apathetic face, altered voice, sensitiveness to cold, and clumsiness of fingers. Oncoming myxœdema was predicted. Death occurred in 1900, preceded by extreme cardiac insufficiency. At the autopsy, marked sclerotic changes were found in the thyroid.

Hirschl[21] discusses the relation between Graves' disease and myxœdema, and reports the case of a woman of thirty-three years, with fairly good history. In August, 1899, symptoms of exophthalmic goitre developed, following a fright; in October palpitation became less, mental hebetude developed, the thyroid became dense, the legs became swollen and hard, and the skin of the face thickened. The left leg was increased in size, smooth, non-pitting, reddish-brown in color; the swelling ended abruptly at the ankle. The right leg was similarly but less extensively affected.

The close pathological relationship existing between myxœdema and scleroderma has been shown by Jeanselme,[22] Singer,[23] and Hektoen.[24] It is not surprising, therefore, in view of what has been said of the association of myxœdema and Graves' disease, to find that occasional instances of the coexistence of scleroderma and exophthalmic goitre are recorded. Grünfeld,[25] in 1896, found three cases in literature; the first by von Luebe in 1875, the second by Kahler in 1888, and the third by Jeanselme in 1895. He himself reports the fourth case. A woman with well-developed Graves' disease was attacked later with scleroderma of moderate severity; a cure was effected with thyroid extract. Osler,[26] in a masterly article on scleroderma, mentions one case associated with Graves' disease. A man of forty years suffered from exophthalmic goitre for two years; the symptoms were typical; scleremic changes then developed in the skin of the legs below the knees. He also records two cases in which tachycardia was present. He found in reviewing the reported cases of scleroderma treated with thyroid, that of ten cases two were cured; seven were improved more or less; and one was not benefited. Dupré and Guillian[27] report a case in a woman of thirty-three years; goitre appeared at thirteen years; exophthalmos at fourteen years; later a clear symptomatology of Graves' disease was recognized; the signs of scleroderma developed at twenty-four years; the hands, forehead, and nose were affected. This patient was of decidedly neurotic type.

Pigmentary changes in the skin have been frequently observed.

Vitiligo is mentioned by Rolland[25] in his thesis as occurring in exophthalmic goitre. Raynaud[29] reports a number of cases. Marie[30] records a case of generalized vitiligo, with areas of brown pigmentation. His description of the spots on the thighs suggests possible telangiectases. Lucy[31] reports a typical case of Graves' disease in which extensive patches of leucoderma were present, as well as areas of brownish pigmentation. The vitiligo began several months before the general disease, but increased greatly during the course of the latter. In this case there was an evident distribution of the patches along the course of the ulnar nerve. Campbell[32] observed a similar combination of leucoderma and melanoderma in three cases of Graves' disease. In all there was a tendency to bilateral symmetry. The pigmentation of the skin may be localized or diffused. Perry[33] reports an interesting case of a woman with exophthalmic goitre who presented a diffuse generalized pigmentation of the skin. There were no evidences of Addison's disease, and under treatment, extending over a period of several months, the bronzing disappeared almost entirely. Burton[34] records a case with pigmentation of the face, neck, axillæ, back, and genitals; Graves' disease was present, but Addison's disease was not excluded. Drummond[35] mentions six cases with localized pigmentation; one showed areas of leucoderma also. Nichols[36] saw a woman and Dore[1] has reported pigmentation and purpura in two different patients, with exophthalmic goitre, in whom large pigmented areas appeared. When Addison's disease is associated with Graves' disease, as in the case of Kruella's,[37] the pigmentation, rather than an anomalous, becomes a cardinal symptom. Other trophic changes have been noted. Among these alopecia is common. Yeo[38] saw a case in which there was falling of the eyebrows, at first unilateral, corresponding to the side presenting the goitre and exophthalmos; later both sides were affected. Barnes[39] reports a case with universal alopecia. Smith,[40] one with general alopecia and glycosuria. In the fifteen cases observed by Mackenzie[9] five showed alopecia in varying grades.

Other dermatoses to be mentioned are urticaria, reported by Bulkley[41] and Rolland;[28] and eczema, observed by Zeleneff.[42] Gangrene of the skin has also been recorded.[28]

In a contribution to the general subject under discussion, where the cutaneous syndromes of exophthalmic goitre have been chiefly considered, the questions of moment respecting the etiology and pathology of Graves' disease may be left to the investigators in the field of inner medicine. At this time it will serve no useful purpose to inquire with scientific precaution into the value of the theories of origin of exophthalmic goitre; whether, for example, there is in these cases a hyperthyroidization; whether there is a primary change in the nervous

centres radiating to the thyroid gland; or whether the gland itself first secretes a toxin, which later acts as an irritant to the nervous centres. By post mortem examinations as well as biopsies of the tissues of the organ, it has been made clear that in many cases after a period of morbid activity the glandular tissue of the thyroid is destroyed by a species of disintegration (cystic, collagenous, colloid, etc.), and that after disappearance of the parenchyma there is left chiefly an hypertrophy of the connective tissue. The persistence of many of the symptoms of exophthalmic goitre after such complete destruction of the secretory tissue of the gland, would militate against the theory of continuous intoxication of the system from that source.

The influence of the nervous centres and nervous tracts in the production of such cutaneous symptoms as the *tache cérébrale* or the lesions of herpes zoster is fully recognized. The established co-existence, in certain cases, of scleroderma and exophthalmic goitre if common etiological factors can be demonstrated for the two, would point to their nervous origin, seeing that the circumscribed (morphœa) type of scleroderma is often displayed in lesions distributed along a single nerve tract; and in the generalized form of scleroderma the early œdematous pitting stage of the disease suggests in a striking manner some of the symptoms of myxœdema, with which disease also, as shown above, exophthalmic goitre is frequently associated. On the other hand the cutaneous symptoms in lepra, though in some instances distinctly traceable to implication of the nerve trunks, as when anæsthetic and hyperæsthetic symptoms can be recognized, may also develop without any alteration of cutaneous irritability to heat and pain, and may thus have their remote origin without question either in the bacilli of lepra or in the toxins of such micro-organisms.

The prime symptoms of exophthalmic goitre are usually enumerated as enlargement of the thyroid gland, exophthalmos, tremor, and tachycardia. Every clinician knows that of these supposedly essential symptoms each in different cases may be wholly absent; so that, notably, a patient with Graves' disease may neither have bulging eyes nor a goitrous swelling. From the point of view of the dermatologist and of the diagnostician, questions of interest arise when, in the absence of one or more of these prime symptoms, dermatoses occur of unusual type or of doubtful origin and relations. Problems of a novel sort would probably be presented to the consideration of a physician confronted with a group of newly-formed bloodvessels in the skin of the face, accompanied by distinct tachycardia, without either exophthalmos or thyroid enlargement; and the same would be true if the cutaneous lesions were those of hidrocystoma, or consisted of two or more morphœa patches on the side of the neck, or of an attack of angioneurotic œdema affecting the general surface of the body.

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NOTES ON THE EMPLOYMENT OF EPICARIN IN TINEA TONSURANS AND TINEA CIRCINATA.

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AND

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EPICARIN was brought into notice several years ago by Prof. Kaposi, of Vienna, as a substitute for naphthol in the treatment of certain diseases of the skin. It is said to be a condensation product of creotinic or creasotinic acid and B. naphthol, and to combine the properties of creasote and naphthol.

Epicarin is a reddish amorphous powder with a slight odor resem-

bling acetic acid. It is soluble in alcohol, ether, and liquid vaselin. It has usually been employed in the form of a 10 to 20 per cent. alcoholic or soda solution, or in the form of ointment of the same strength.

Kaposi employed it at first in the cure of scabies. Eighty cases were treated with excellent and rapid result. He also employed it in a certain number of cases of ringworm, and in prurigo of children with similar good results. In eczema and psoriasis it is said to have proved irritating.

Pfeifenberger found that where much dermatitis was present with scabies, epicarin proved somewhat irritating. In 7 per cent. ointment form he found that the scabies could be cured, but that the attending dermatitis required more soothing remedies.

Pfeifenberger employed epicarin in the case of children, from one to fourteen years of age, without finding any untoward effect upon the kidneys, such as sometimes accompanies the use of B. naphthol. In scabies the severe itching diminished after the first or second inunction, in most cases; the skin, however, became red, dry, and rough, showing superficial fissures here and there.

To prevent irritation of the skin in the treatment of scabies, the epicarin was stopped after having been used every night for three nights, and a soothing ointment, such as ung. diachylon, was applied for several days. Then a bath was ordered. This carried off the superficial scaly skin and with it the itch mites. No application was made for three or four days, at the end of which time, if any spots showed disease, fresh inunctions of epicarin were employed. Five or six generally proved sufficient.

The treatment completed, the skin presented a smooth, soft texture with a shiny aspect and a reddish color. This staining or coloration lasted for some time after the cessation of the treatment. It may be mentioned that the epicarin treatment was applied immediately, no bath preceding treatment.

The maximum length of time required for a cure was not more than nine days, the delay being caused by the concurrent dermatitis, which had to be handled carefully. Prurigo in children was likewise treated by epicarin with excellent effect.

In addition to the 10 to 20 per cent. alcoholic solution of epicarin the following ointment, chiefly employed in the scabies cases, was used:

℞ —Epicarin	7	grm.
Cretæ albæ	2	"
Vaselini albæ	30	"
Lanolin	15	"
Axungiæ porci	45	" —M.

The material employed in our investigations was derived chiefly from the out-patient department of the Children's Hospital of this city, and was subject to the vicissitudes usually experienced in such clinics. The solicitude shown by the parents, whose children were deprived of

school privileges during the presence of ringworm on the scalp or body, fortunately afforded us more opportunities for following the course of treatment than are usually permitted.

After examination and diagnosis of each case, the hair was clipped or shaved around the neighborhood of the patches, or in some cases, where the disease was diffuse, the entire scalp was shaved. The scalp was then carefully gone over and the tincture of epicarin was vigorously rubbed into every suspicious patch of skin. The parent was provided with some of the same tincture, or in some cases with the ointment, and was told to rub it well into the scalp wherever any diseased spots could be found, once or twice daily. In some cases a germicide soap was also employed to shampoo the scalp daily, in order to prevent the accumulation and diffusion of dry scales containing the ringworm fungus.

In all cases thus treated the personal equation of the nurse or attendant counts for very much. We found that the few cases treated in the hospital wards by skilled and intelligent nurses were cured much more rapidly than those committed to the hands of less intelligent mothers for home treatment. Even here, however, it was found that the greatest difference in results obtained between intelligent and anxious parents and those who were lazy and indifferent.

The number of cases, though much greater in total than those reported, was still insufficient to allow the employment of a great variety of preparations of the drug. We mostly used the preparations as described by Kaposi; that is, the 10 and 20 per cent. tincture and ointment. The tincture seemed decidedly the most efficient preparation. Used in the ward cases immediately after depilation the effect was surprising. In one very recent case a cure was effected within ten days. On an average, five weeks were required to bring the disease to an end.

Although few microscopic examinations were made, it is believed that in each case the fungus involved was the large-spored variety, and that no cases of the small-spored and more inveterate form of fungus came under treatment during the period of our investigation.

Only a few cases of scabies came under observation, and of these only two were treated with epicarin. The formula used was that of a simple 10 per cent. ointment with a base of petrolatum. The result was quite unsatisfactory; the ointment irritating the skin quite severely and not producing much impression upon the disease nor giving much relief from the accompanying pruritus. On changing to the ointment of naphthol and sulphur as usually employed in the skin clinic of the Children's Hospital, very speedy relief was experienced. It is possible that if the compound epicarin ointment, as given above, had been employed, somewhat better results might have been obtained. The old treatment, however, is so satisfactory that it seems hardly worth while to try epicarin further in the treatment of scabies.

TABLE OF CASES TREATED WITH EPICARIN.

Case.	Duration.	Description.	Treatment.	Remarks.	Result.
1	3 wks.	Tinea tonsurans. Two lesions on scalp, half-dollar size, covered with short hairs with an ash-like gray appearance.	Tinct. epicarin, 10 per cent.	.....	Improved.
2	3 wks.	Tinea circinata et tonsurans. Two coin-sized patches on scalp, rough nutmeg grater appearance; some hairs broken off short; others, including those in neighborhood of patches, long but pulling out readily; also patches of tinea circinata.	Germicide soap and epicarin ointment, 10 per cent.	Tinct. epicarin, 10 per ct., applied in clinic.	Improved.
3	3 wks.	Tinea circinata et tonsurans. One patch on scalp; most hairs long, but many loose; tinea circinata also.	Germicide soap and epicarin ointment, 20 per cent.	Tinct. iodine had been employed previously, but without satisfactory result; under treatment two weeks.	Improved.
4	6 days	Tinea circinata. Confined to face; chiefly right side; characteristic rings of vesicular ringworm; some dozen lesions in all.	Tinct. epicarin, 10 per cent.	Two visits to the clinic sufficed to cure this case.	Cured.
5	Some months	Tinea tonsurans. Three or four small infiltrated patches on scalp.	Ung. epicarin, 10 per cent.	The ointment was rubbed in daily, while the tinct. epicarin was applied on his visits to hospital; under treatment two months.	Cured.
6	4 mos.	Tinea tonsurans. Well-marked case; large ash-colored rough patch on back of scalp; irregular patches not so characteristic elsewhere.	Tinct. epicarin, 10 per cent.	Only paid one or two visits.	Improved.
7	3 wks.	Tinea circinata. Three coin-sized patches on scalp and several ring-shaped lesions; tinea circinata of arm.	Tinct. epicarin, 10 per cent.	Epilation was also practised; ceased attendance.	Improved.
8	2 days	Tinea circinata. One lesion on forehead coin-sized.	Tinct. epicarin, 10 per cent.	Treated daily; eruption disappeared in seven days.	Cured.
9	2 days	Tinea circinata. One lesion on knee.	Tinct. epicarin, 10 per cent.	Treated daily; eruption disappeared in fourteen days.	Cured.
10	3 days	Tinea circinata. Several small-ringed lesions on right temple, under chin and on trunk.	Tinct. epicarin, 10 per cent.	Failed to report.	Cured?
11	.....	Tinea circinata et tonsurans. Large oval ring on left leg above knee; some lesions on scalp.	Tinct. epicarin, 10 per cent.	At the end of seven weeks the lesion on knee was reported well; it had probably been so for some time. The scalp lesion was nearly well at the end of ten weeks.	Cured.
12	11 mos.	Tinea tonsurans. Three or four coin-sized patches and a large number of smaller patches in scalp.	Tinct. epicarin, 10 per cent.	The epicarin was applied three times weekly after epilation at clinic, and at home daily; duration six weeks.	Cured.
13	1 mo.	Tinea tonsurans. One coin-sized incipient patch on left side scalp, also a patch of "alopecia areata."	Tinct epicarin, 10 per cent.	At the end of four weeks seemed well.	Cured.
14	.....	Tinea circinata. Very marked eruption, chiefly over face, neck, arms, legs, and body; lesions ringed.	Tinct. epicarin, 10 per cent.	After several days' treatment decidedly better; patient disappeared.	Cured?
15	.....	Tinea circinata. Distinctly ringed lesions, chiefly on face and ear.	Tinct. epicarin, 10 per cent.	After several days' treatment decidedly better, ceased attendace.	Cured?
16	1 week	Tinea tonsurans. Coin-sized lesion on scalp.	Tinct. epicarin, 10 per cent.	....	Improved.

Case.	Duration.	Description.	Treatment.	Remarks.	Result.
17	1 week	Tinea tonsurans. Small patches on scalp.	Tinct. epicarin, 10 per cent.	.....	Improved.
18	3 mos.	Tinea tonsurans. Scalp pretty well covered with large and small patches.	Tinct. epicarin, 10 per cent. Ung. epicarin.	The scalp was shaved and tincture was applied thrice weekly at the hospital, the ointment being applied at home daily; duration of treatment two months.	Cured.
19	2 wks.	Tinea circinata et tonsurans. Palm-sized patch over right ear, and smaller one on top of scalp.	Tinct. epicarin, 10 per cent. Ung. epicarin, 20 per cent.	Shaved; salicylic collodion to face lesions; afterward ung. epicarin; tincture to scalp; under treatment six weeks.	Improved.
20	1 mo.	Tinea circinata. A single ring-shaped lesion on nose and adjacent skin.	℞.—Epicarin, gr. v. Ung. zinc oxid., 5iv.	Treatment about a week.	Cured.
21	3 wks.	Tinea circinata et tonsurans. Lesions on chin, face, and scalp.	Tinct. epicarin, 10 per cent.	Treatment three weeks.	Cured.
22	2 wks.	Tinea circinata et tonsurans. Two patches on scalp, one over right eye.	Tinct. epicarin, 10 per cent.	The patch over right eye was well in two weeks; the scalp in three months.	Cured.
23	3 mos.	Tinea circinata et tonsurans. Quite extensive; nutmeg grater patches on scalp.	Tinct. epicarin, 10 per cent.	This case was severe and extensive, but was nearly cured at the end of three months.	Improved.
24	2 mos.	Tinea circinata et tonsurans. Small, round, elevated patches on scalp.	Tinct. epicarin, 10 per cent.	At the end of two months healthy hairs growing everywhere.	Improved.
25	.....	Tinea tonsurans. Two coin-sized superficial patches on scalp.	Ung. epicarin, 20 per cent.	At the end of three weeks practically well.	Cured.
26	2 mos.	Tinea tonsurans. Well-marked tendency to crusts.	Ung. epicarin, 20 per cent.	The ung. epicarin was said to have produced pustules; however, it was continued and the tincture used on visits to hospital; in seven weeks practically well.	Cured.
27	.....	Tinea circinata. Vesicular ringworm of wrist, smaller lesions elsewhere.	Tinct. epicarin, 10 per cent.	When the tincture of epicarin seemed too irritating an aristol ointment was used for a short time.	Cured.
28	.....	Tinea tonsurans. Light, thin hair; extensive scaliness through scalp; tendency to round patches.	Tinct. epicarin, 10 per cent.	Under treatment five weeks.	Cured.
29	.....	Tinea circinata. A single lesion two centimetres in diameter on right wrist.	Tinct. epicarin, 10 per cent.	At first seemed to increase in size, but soon began to improve rapidly; under treatment three weeks.	Cured.
30	3 wks.	Scabies. Three weeks' duration; well marked on body and limbs.	Ung. epicarin, 10 per cent.	The epicarin ointment was employed for about three weeks; it may have acted favorably, but it proved so irritating that it was changed for a naphthol and sulphur ointment, which acted more satisfactorily	
31	2 wks.	Scabies. Well marked; hands and arms chiefly affected.	Ung. epicarin, 10 per cent.	The epicarin seemed irritating and not very effective; probably recovered under use of naphthol and sulphur ointment as used by 30.	

The conclusions we have reached are as follows:

1. In epicarin we have an important addition to the means of combating ringworm of the scalp. Used, preferably, in the form of a tincture of 10 to 20 per cent. strength and after epilation it appears to act more rapidly than any of the remedies heretofore employed, in restoring the hairs to a normal condition.

2. In ringworm of the body the tincture seems to be irritating and slow in action. The ointment acts better, but is not equal to the ammoniated mercury ointment, nor to most of the remedies ordinarily employed.

3. In (a single case of) favus the result of the use of epicarin was such as to encourage trial.

4. In scabies, so far as our experience goes, epicarin in the form of the tincture and simple ointment is apt to prove very irritating, and is by no means equal to the sulphur and naphthol nor to the other ointments ordinarily employed.

THE BLOOD-PRESSURE REACTION OF ACUTE CEREBRAL COMPRESSION, ILLUSTRATED BY CASES OF INTRACRANIAL HEMORRHAGE.

A SEQUEL TO THE MÜTTER LECTURE FOR 1901.

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Some experimental observations on the rôle played by the vasomotor centre in raising the arterial tension so as to counterbalance the effects of any considerable increase in intracranial tension were presented as part of the Mütter lecture[1] in December, 1901. Since then opportunities have arisen which have made it possible to demonstrate in clinical cases reactions corresponding to those which at that time had only been experimentally produced in animals. To review some of these cases is the purpose of this communication.

It is a well-recognized clinical fact that the rapid[2] encroachment on the intracranial space by a foreign body, of which extravasated blood may be taken as one of the commonest types, is associated with a high tension pulse. Similarly the laboratory experience of many investigators has shown that a transient great rise in blood pressure is an almost uniform accompaniment of artificially induced compression. I

[1] The Mütter Lecture for 1901. The American Journal of the Medical Sciences, September, 1902, vol. cxxiv. p. 375.

[2] In a slowly forming intracranial process, as tumor growth, hydrocephalus, etc., the reactions are inconspicuous, the cerebrum accommodating itself to the gradual increase of tension.

am unaware, however, that any especial interpretation has heretofore been given to this response other than that it represented some aimless or uncontrolled action, from irritation of the vasomotor centre during a certain stage of increase of tension within the cerebral chamber.

The experiments above referred to, which for the most part were carried out upon dogs, tended to show, if the interpretation were a correct one, that this rise in blood pressure represents a purposeful and not a meaningless reaction.[1] The belief was expressed in a regulatory mechanism which controls the rise, and which, under experimental circumstances at all events, is seemingly so adjusted that the vasomotor centre tends to hold the intravascular pressure (arterial tension) at a level slightly in excess of the external (extravascular) pressure exerted by the compressing force against the arterioles and capillary vessels situated in the medulla. In this way a fatal bulbar anæmia, which otherwise would be the result of an equalization of intracranial and a stationary arterial tension, is warded off. Thus, the high-pressure pulse, which characterizes conditions of intracranial hemorrhage, for example, is easily accounted for, and its measured level of tension may be taken as an indication of the degree of circulatory embarrassment from which the medulla is suffering in consequence of the compressing force. It was pointed out that under these circumstances the continuance of respiration hinged upon the efficiency of the vasomotor mechanism in holding the blood pressure at a certain level. Should the vasomotor centre fail to keep the arterial tension in excess of the experimentally increased intracranial tension, the respiration would immediately cease, owing to the anæmia of the centre governing it. Consequently, as will be emphasized in the discussion of some of the following cases, the sequence of events in case of immoderate intracranial tension is, primarily, exhaustion of the vasomotor mechanism with fall in blood pressure, and, secondarily, failure of respiration in consequence of the ensuing bulbar anæmia.[2]

[1] In a note appended to an article by the writer in the Mittheilungen a. d. Grenzgebieten d. Med. u. Chir., 1902, Bd. ix. p. 773, in which this experimental work was reported at some length, one of the editors (Naunyn) states that this rise in blood pressure during compression had been noted and described by himself and Schreiber in their well-known monograph, "Ueber Gehirndruck," published twenty years ago. (Arch. f. experim. Pathol. u. Pharmakol. 1881, Bd. xiv. p. 1.) I regret having made no reference to the contents of this classical paper. As a matter of fact, however, this reaction has been noted by almost all experimenters who have worked along these lines, and the rise in blood pressure on which most stress is laid by these particular writers is that which occurs early in compression, the "primäre Erhebung," which is a result of sensory irritation, and not the subsequent and long-enduring rise from anæmia which we are discussing. The failure to record the degree of intracranial tension on the kymograph alongside of the blood pressure probably explains why previous observers have failed to recognize what seems to be the true significance of the rise in blood pressure. Prof. Naunyn expresses some doubt as to the correctness of the interpretation which was offered, namely, that of a "Regulationsmechanismus." Future observations will settle the point.

[2] This relationship of the respiratory action to blood-pressure levels and to the degree of intracranial tension was especially well shown in cases in which vasomotor (Traube-Hering)

In the majority of circumstances the vagus centre is likewise stimulated under the effects of compression with the resultant familiar slowing of pulse rate, which, however, does not seem to bear so definite a relation to the degree of increased tension. Aside from the fact of its frequent concomitance the brachycardia does not apparently play any particular part in the reaction under discussion, nor can it be always said that the more advanced the compression the slower will be the pulse rate.

The significance of this vasomotor regulation, should it have been possible to establish it as true for man as well as animals, was fully realized, but, unfortunately, at the time the Mütter lecture was prepared, no opportunity had been offered on clinical cases to satisfactorily corroborate the laboratory findings, much less to put the facts to any practical application.

The introduction for clinical purposes of a simplified form of the original Riva Rocci blood-pressure apparatus has enabled us to take observations on arterial tension, and to plot them on charts which simulate in a useful way the invaluable records which in the laboratory may be obtained by taking blood-pressure records directly from an isolated vessel. By employing this apparatus it has been possible to chart graphically the blood-pressure reaction in several cases of intracranial injury, and thus to bring clinical cases in line with the experimentally induced conditions. The results have proven of such interest and the method of observation of such practical value that it is hoped the few cases, which will subsequently be given at some length, may suffice to further illustrate the points which the experimental work has brought out.

Prof. Kocher,[1] in his recent monograph, has for the sake of convenience divided into several stages the period between the first onset of compression symptoms and the terminal paralysis which may end the story. These stages, corresponding as they do to a given degree of circulatory disturbance consequent on the increase of tension, have individually a more or less characteristic and distinguishable symptom-complex. The process, of course, may come to a standstill in any one of the various stages. Kocher's classification is a most useful one, and inasmuch as the cases, which have been selected, conform with and exemplify the divisions which he has drawn, the latter will be briefly outlined.

waves were called out. Under these circumstances active respiratory action corresponded to the crests of the waves—that is, to *periods of blood pressure exceeding in degree the intracranial tension;* whereas the hollows of the waves during which *the blood pressure fell below the intracranial tension,* with resultant temporary anæmia, invariably corresponded with periods of respiratory cessation.

[1] Hirnerschütterung, Hirndruck u. s. w. Nothnagel's Specielle Pathologie und Therapie, 1901, Bd. ix., Thiel 3, Abt. 2, p. 186.

STAGE I. ("*Compensationsstadium.*") The first stage, that of circulatory compensation, corresponds to an early period or mild degree of compression, during which the encroachment on the intracranial space, by some foreign substance which displaces the normal contents of the cerebral chamber, is not sufficient to seriously compromise the circulation. By the escape of cerebrospinal fluid and by a certain amount of narrowing of the venous channels, the process is accommodated with the avoidance of any pronounced degree of venous congestion of the brain. Under these circumstances symptoms, although not absolutely latent, are in the main insignificant.

STAGE II. ("*Anfangsstadium des manifesten Hirndruckes.*") If the process continues to the point of failure of this circulatory compensation a condition of venous stasis is brought about, with a lessening of the normal amount of blood flowing through the capillaries (Dysdiämorrhysis). At this time symptoms of disturbed cerebral function are inaugurated evidencing an early stage of actual compression—headache, vertigo, restlessness, roaring in the ears, a disturbed sensorium with excitement or delirium, an unnatural sleep, etc. Other symptoms also become outspoken. Among these, of highest importance is the recognition by means of the ophthalmoscope of some distention and tortuosity of the veins radiating from the optic papilla; indeed, a certain degree of venous stasis may have been appreciable in the eye-grounds during the previous stage of compensation. Indications that the venous congestion is influencing bulbar circulation may be apparent as a slowing of the pulse with or without a certain rise in blood pressure.

STAGE III. The third stage, that of advanced compression phenomena ("*Höhestadium des manifesten Hirndruckes*"), corresponds to a condition of capillary anæmia due to a further increase in intracranial tension. This anæmia in case of "local compression" may have exerted its effects primarily over a circumscribed area of the cerebrum, throwing out of function that part of the brain in its vicinity with corresponding paralytic symptoms. Should, however, the pressure from such a local process be sufficiently far-reaching to involve the medulla, or should the medulla from the start have been involved in the threatened anæmia in correspondence with the rest of the intracranial contents (that is, in case of "generalized compression"), then the period of vasomotor regulation follows with its characteristic rise in blood pressure. This reaction may last an indefinite period, until relief is afforded or until an increase in compression is more than can be compensated for, and the terminal stage of compression steps in to supplant it. Associated with the rise in blood pressure may be seen marked respiratory disturbances, which are especially distinctive when the former is accompanied by rhythmic alterations in level. The periodicity of symptoms so often observed during this stage, and refer-

able not only to respiration, but shown also by rhythmic alterations in size of the pupils, by wavering increase and diminution in depth of stupor, and by many other signs indicative of alterations between irritative and paralytic symptoms, is due to this vasomotor rhythm associated as it is momentarily with sufficient cerebral circulation (Eudiämorrhysis) alternating with a period of inadequate or totally deficient blood supply (Adiämorrhysis).

Vagus symptoms are, as a rule, pronounced during this stage, the pulse being slowed to 50, 40, or even fewer beats per minute, but without, or, at all events, with much less apparent evidences of rhythm.

Stage IV. The terminal stage ("*Lähmungsstadium*"), which follows upon an increase of intracranial tension over and above that which can be compensated for by stimulation of the vasomotor centre, is characterized by a falling blood pressure, irregular cardiac and respiratory efforts, deep coma, which supplants the varying degrees of stupor, complete muscular relaxation, wide pupils, broken, snoring respiration, etc., soon to terminate in cessation of all cerebral function, with respiratory paralysis and with the rapid pulse of low pressure, indicating failure of the vasomotor mechanism. An irrecoverable condition of cerebral anæmia (Adiämorrhysis) has been reached.

In this brief characterization of the stages of compression only the main features of the symptom-complex have been cursorily reviewed. In case any one of these stages of circulatory disturbances has been brought about by a compressing force primarily local in origin, the symptoms naturally would vary greatly, from case to case, as the important underlying symptoms referable to the medulla are surmounted by others, called out by paralysis or irritation of those parts of the cortex primarily subjected to the local process. It would not only carry us too far to discuss this superstructure of symptoms here, but be inappropriate, since the cases to follow have been selected to illustrate solely the vasomotor reaction, and it is desirable to avoid as far as possible any complexity in the clinical picture.

These cases are reported from the neurological department of Dr. Halsted's clinic. They may be briefly summarized as follows:

Case I.—Traumatic in origin. One of local compression of considerable degree, not sufficient, however, to compromise the intracranial circulation, and being over a "silent area" of the cortex, giving practically no evidence of its presence. It illustrates the "Compensationsstadium" (Stage I.) of compression with only latent symptoms and no rise in blood pressure.

Case II.—Traumatic in origin. One presumably of general increase in intracranial tension from intermeningeal hemorrhage. It illustrates the beginning period of bulbar involvement (Stage II.), and shows how blood-pressure observations may be utilized as an indication for or against the necessity of operation. The rise in blood pressure

compensated for the compressing force at a relatively low and safe level.

CASE III.—Traumatic in origin. Extensive intracranial hemorrhage progressively increasing until symptoms of the "Höhestadium des manifesten Hirndruckes" (Stage III.) were produced. The indications for operative interference were shown by a steady rise in blood pressure in correspondence with the general increase of compression until a point was reached at which failure of compensation was feared. Symptoms of local compression superimposed on the main underlying ones.

CASE IV.—Apoplectic; also illustrating Stage III. Hemorrhage into the internal capsule. Characteristic symptoms of the supreme reaction of compression with great elevation of blood pressure, indicating the borderland of the paralytic stage. Immediate relief to underlying major symptoms of compression by craniotomy and partial evacuation of clot.

CASE V.—Traumatic in origin. Illustrating Stage IV., the "Lähmungsstadium." A case of fatal compression from intracranial hemorrhage with primary vasomotor and secondary respiratory failure. Operation performed during artificial respiration.

CASE I. (Surgical No. 13,658.) *Compound fracture of os frontalis, with extensive extradural hemorrhage and with no major symptoms of compression; operation.*—The patient was admitted through the accident room on the night of July 31, 1902, with the history of having been struck on the forehead by a six-pound iron hammer three hours previously. He was not knocked down by the blow. There had been no period of unconsciousness, nor had he shown any symptoms whatever of concussion. After his entrance he complained of nausea, and vomited twice. This was attributed to the alcohol he had taken, for he was somewhat inebriated. He complained only of severe "headache."

There was a small lacerated wound near the midline of the forehead, through which a crack in the frontal bone was detected. Beyond this a careful examination was absolutely negative. The eye-grounds were not examined. He was perfectly rational, and had complete recollection of all incidents relating to his injury.

On the following morning his condition was unchanged. He had slept well during the night. His mind was clear, and memory of the events of the preceding night accurate. Examination again failed to reveal any objective symptoms referable to intracranial disturbance. His pulse, respiration, temperature, and blood pressure were normal. The pain in the head was less severe.

Operation, August 1st. Dr. Watts. Ether anæsthesia. After excising the external lacerated wound, exploration of the underlying skull showed a small comminuted and depressed fracture involving both tables. On elevating and removing the fragments a large, underlying, extradural blood clot was brought to view. This hemorrhage was fully exposed by the further removal of bone, and was found to correspond to an area about 7 × 9 cm. in diameter underlying the frontal bone and extending symmetrically on the two sides. It was estimated that about 100 c.c. of extravasated blood was present. The clots were removed with a spoon, the wound washed clean, and a small drain

inserted. The patient's recovery, except for a slight slowing of the pulse for a few days, was uneventful. There was an immediate post-operative relief from the pre-existing headache.

Discussion. The possibility of a considerable narrowing of the intracranial space by an acute process without the production of stereotyped compression symptoms is well exemplified by this case. It is evident that the major or underlying symptoms of compression need not be provoked by an extradural hemorrhage of considerable size if it be in a favorable situation, and, furthermore, that the local pressure effects of the process need not be productive of minor and localizable paralytic or irritative symptoms if they are exerted over so-called silent areas of the cortex. The clot made room for itself by pressing the cerebrospinal fluid out of the cranial cavity and presumably by narrowing the venous radicles in its vicinity without otherwise compromising the intracranial circulation.

An extradural hemorrhage in this situation must needs have been very extensive and under great tension to have transmitted its effects without any associated concussion, to so remote a situation as the bulb, thus causing a slowed pulse and rise of blood pressure. Being over the frontal lobes, moreover, it failed to give appreciable symptoms indicating local disturbance of cortical areas, such as would have been present had the clot formed, for instance, over the motor territory. No psychic symptoms were detected. The circulatory disturbances of the brain due to the pressure of the foreign body and doubtless occasioning a certain amount of anæmia in its immediate vicinity over the frontal lobe were not sufficiently far-reaching to involve any important centres. Possibly had an examination of the fundus been made some degree of stasis might have been made out in the eye-grounds. The pain and headache complained of were practically the sole symptoms, and were undoubtedly of dural origin. In the lower animals especially is the dura found to be a most sensitive structure. Even under anæsthesia an attempt to strip away the membrane from the skull during experimental procedures on dogs will cause pronounced irritative symptoms. Clinically an extradural hemorrhage plays the same rôle, and may be productive of the most severe dural pain and headache. It is interesting to note in this connection that should individuals have headache after extirpation of the ganglion semilunare the pain, in my experience, at least, is invariably unilateral, and referred to the unoperative side, where the dura retains its sensation. In this case, as is usual, the headache was immediately relieved by the removal of the clot.

Among our recent series of cases of cranial injury, in no other instance has a moderate degree of compression been present, uncomplicated by symptoms of concussion. Hence, this case has been chosen

to illustrate the compensation stage. Several cases of fracture of the base with intermeningeal hemorrhage and slight increase of intracranial tension, as told by lumbar puncture, have been seen and found likewise to be unassociated with bulbar symptoms. The element of concussion, however, has always been present in these cases, and has more or less obscured the symptoms which the compression alone might have caused. This combination of pressure factors will be considered in the following case:

CASE II. *Simple fracture of the base; concussion and mild degree of compression from intermeningeal hemorrhage; lumbar puncture; no operation.*—The patient was admitted through the accident ward, April 12, 1902, with the history of having been struck under the jaw two hours previously by a swinging, heavy, steel rail. The blow felled him to the ground, with momentary loss of consciousness.

The note, made on admission, reads as follows:

"A powerful working man, with a large head, a strongly developed lower jaw and facial bones. He lies in a stuporous sleep most of the time, with occasional interruptions of active restlessness. He can be aroused somewhat by the infliction of pain (supraorbital pressure), but will not respond to questions, and relapses immediately into his previous somnolent condition.

"His pulse is 69, regular, and of fairly high tension to palpation. The arterial pressure at the brachial measures 160 mm. of Hg. The respiration is deep, regular, and 24 to the minute. The temperature is subnormal, registering 97° per rectum. On the left side of the chin below the mental prominence is a small, contused, bleeding wound. No fracture of the powerful inferior maxilla can be made out. The jaw can be moved in all directions, apparently without pain. Pressure on the chin, however, causes the patient to wince, apparently from transmission to the skull. The right margin of the tongue has been almost bitten through. There is considerable bleeding from the right ear. Pressure over the supramastoid ridge on the right side gives evidence of great tenderness. There is no bleeding from the left ear or apparent tenderness anywhere on that side of the head.

"The pupils are equal, contracted to a diameter of 2 mm., and react to light. There is a marked divergent strabismus. The veins of the fundus, examined after dilatation of the pupil with cocaine, seem considerably dilated. The supraorbital reflex is very active on both sides.

"The deep reflexes at the knee and ankle are considerably exaggerated and equally so on both sides. There is a prompt dorsal flexion of the great toe on each side in response to plantar stimulus. During the examination the patient has retched violently, but without vomiting.

"In the half-hour since admission the pulse rate has gradually dropped from 69 to 63 beats per minute, and the blood pressure has correspondingly and gradually risen from 160 to 185 mm. of Hg."

A lumbar puncture was subsequently performed, and 24 c.c. of bloody fluid under 23 cm. (water) tension was withdrawn, being a conclusive evidence of basal fracture with some intermeningeal hemorrhage and increase in intracranial tension.

As the accompanying chart (Fig. 1) shows, frequent observations on the pulse rate and arterial tension were taken during the day, and

inasmuch as there was no further increase in the latter beyond the 185 above recorded and considered a safe level, it was concluded that there was no indication for operative interference.

Symptoms, attributable largely to the effects of concussion, were present in this case—headache, nausea, dizziness on assuming an erect posture, etc.—all of which gradually subsided during the ten days following the accident, and *pari passu* with the return of the blood pressure and the pulse rate to their normal level (see Fig. 1). Doubtless the two conditions—concussion together with an increase of tension due to the intermeningeal hemorrhage—were combined, the latter showing itself as an early rise in blood pressure, the former as a late rise in

FIG. 1.

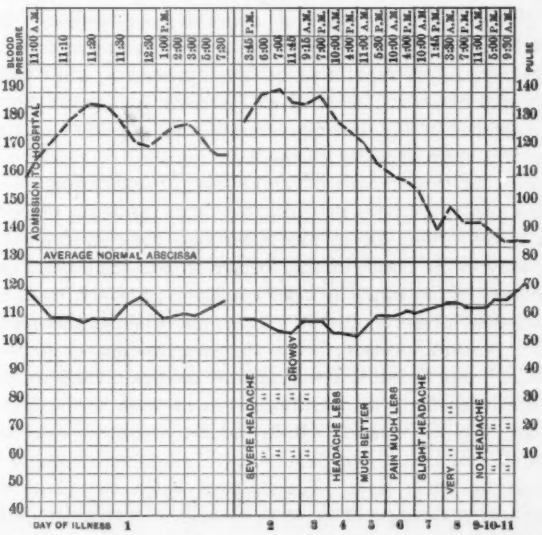


Chart of blood pressure (broken line) and pulse rate (solid line) in Case II. Note the increment in arterial tension and diminution of pulse rate on the day after admission, with gradual return to the normal during the ten succeeding days.

association with a certain degree of slowly-forming cerebral œdema, possibly of the type which Cannon[1] has ascribed to osmotic pressure, "which in brain tissue may attain a degree so much greater than blood pressure that the blood would readily be prevented from entering the cranium."

DISCUSSION. In this case the blow had been transmitted directly to the base of the cranium through the arch of the lower maxilla just as in the so-called "prize-fighter's fracture" of the skull—a form of injury not infrequently followed by a fatal outcome. The fracture

[1] Cerebral Pressure following Trauma. American Journal of Physiology, 1901, vol. vi. p. 91.

passed through the middle fossa and the temporal bone, and some degree of subdural hemorrhage ensued. A hemorrhage of this sort into the subdural space produces a condition which resembles as closely as do any other clinical ones the experimentally induced conditions of general compression—that is, conditions in which there is an equal distribution of increased tension throughout the entire cerebral chamber. The case is a representative one of a degree of cranial injury so frequently met in a traumatic service that it must be familiar to all. Under the circumstances no operation was performed, since it could have done nothing more than relieve intracranial tension, and there was no indication that this was necessary, since the process was arrested at a stage ("the beginning stage of manifest compression") in which there could have been no apprehension lest the vasomotor centre become fatigued in its regulation of blood pressure. Had the process advanced and given evidence of still greater tension, as shown by a further increase in the blood-pressure level, operative intervention might have become urgently demanded.

The effects of "compression" and those of "concussion" in a traumatic case are ordinarily distinguishable, in so far as the blood-pressure reaction is concerned, for in the latter case the rise, if one there be, will be tardy in its onset, in the former rapid. The occasion of the rise, however, is the same in both conditions, namely, an increase in the intracranial pressure, and it matters not whether this results from so-called "cerebral pressure" due to brain œdema, or to "cerebral compression" due to forces acting against the brain from without.

The beneficial effects of operations even in these border-line cases is often seen. On one occasion within the last year two young men, who had been thrown in a motor-paced bicycle race, were brought into the hospital at the same time. The injuries which they had sustained were practically corresponding ones, namely, a cranial fracture (compounded in one case) with some intermeningeal hemorrhage, as evidenced by lumbar puncture. Both patients were suffering from a pronounced degree of concussion. The low blood pressure registered in each case at the time of admission showed that there was no increase in intracranial tension. The compound case was operated upon by Dr. Follis, who elevated the fragments, and during the operation exposed the brain by an opening in the dura. The cerebral cortex was so ecchymotic as to present a cherry-red color, but gave no evidence whatever of an increase of tension. A piece of bone was permanently removed and the wound closed. This patient made a rapid recovery, showing none of the usual delayed post-traumatic signs of concussion, and after the first twenty-four hours was without subjective symptoms. The other, the unoperated case, remained in a more or less stuporous condition for several days, with headache, nausea, a rise in blood

pressure, and slowing of pulse, which gradually shaded off to the normal after a period of many days—a reaction which is frequently seen after cases of concussion (see Figs. 1 and 3).

Although far from advising operation in every border-line case of basal fracture with concussion, especially when blood-pressure observations show no great increase in intracranial tension, it nevertheless is evident from our records that, given two patients with supposedly similar lesions, the operated case with an opening left in the skull makes a more rapid recovery than the non-operated one, and, furthermore, seems to be less likely to suffer from the post-traumatic sequelæ of epilepsy and late mental derangements.

In the discussion of Case I. it has been noted that a local process even of considerable extent may call forth no symptoms characteristic of compression. If, however, such a process becomes more advanced so that its effects in upsetting the circulation are transmitted as far as the medulla, compression symptoms will be evoked. Unfortunately, for purposes of illustration, there is no case in my series in which a purely local process, as from an extradural hemorrhage, has inaugurated but not advanced beyond (as in Case III.) the early symptoms of medullary involvement. An analogous condition, however, is frequently seen during certain operative procedures which necessitate the elevation and compression of a lobe of the brain during extradural manipulations. Thus, the slowing of pulse and rise in blood pressure, which often accompanies the elevation of the temporal lobe in the Gasserian ganglion operation, has been emphasized heretofore and illustrative charts given.[1] The operative procedure on such an occasion becomes the equivalent of an experimentally induced compression carried to the "Anfangsstadium des manifesten Hirndruckes."

Case III. (Surgical No. 13,260.) *Simple linear fracture of the skull, vault and base, without concussion; extradural hemorrhage from rupture of A. meningea media; also, intermeningeal hemorrhage; severe compression symptoms; operation; recovery.*—The patient, a young man aged twenty-four years, a ship's carpenter by trade, was brought to the accident ward on April 17, 1902.

One hour before his admission, while directing the lodgement of a heavy piece of timber under the hull of a vessel, in some accidental fashion the beam slipped, and the patient's head was caught between it and the side of the boat, crushing the skull in "nut-cracker" fashion. He fell to the ground, bleeding from his nose and both ears. He did not immediately lose consciousness, as in cases of cerebral injury with concussion, but gathered himself together, stood up, and for some moments was able to ask and answer questions about the injury. During the course of the next half-hour he became gradually stuporous, and was brought to the hospital in an unconscious condition.

[1] Blood-pressure Changes in Surgical Cases, etc. Annals of Surgery, September, 1902.

The following note was dictated soon after his admission, 4.40 P.M.: "The patient is a well-developed young man. He is unconscious, and cannot be aroused by questions. He is restless and seemingly annoyed, reflexly, by slight peripheral stimuli, such as are occasioned by the taking of pulse and blood pressure, by the blood in his ears and nose, at which he is constantly picking. His pulse is 56 to the minute and of high tension. The respiration is 30 to the minute and regular. The blood pressure is high, measuring 230 mm. of Hg.

"*General Appearance.* The skin over the head, face, and neck is markedly cyanosed. Several veins over the forehead are prominent and of a deep-blue color. The eyelids seem swollen, as from congestion, and the network of venules over them is very evident. There is an apparent slight exophthalmos. The pupils are quite unequal, the right being almost pin-point in size, the left measuring 4 mm. in diameter. The axes of the globes are rarely quite parallel; at times, however, there is an equal conjugate deviation to the left.

"The only visible wound consists of a lesion of the right external ear, the pinna having been torn or rather crushed into two separate portions. There is marked tenderness on pressure over the temporal bone in the neighborhood of the ear, and there are beginning ecchymoses in this situation. Over the left parietal eminence the scalp is bruised and slightly swollen. There is considerable bleeding from the auditory meatus on both sides. Slight twitching of the muscles on the right side of the face is occasionally seen.

"The deep reflexes are possibly somewhat exaggerated with a suggestion of ankle clonus. No plantar response obtained. The temperature is 98.4°. The patient is not in a condition of shock."

An examination of the eye-grounds showed what was taken to be a marked dilatation of the veins.

During the hour subsequent to the making of this examination the patient's condition slowly but perceptibly changed for the worse. His stupor deepened, and he was much less easily aroused. The blood pressure rose steadily from 230 to 250 mm. of Hg., and the pulse meanwhile dropped, occasionally registering less than 50 beats per minute (compare chart, Fig. 2). The character of the respiration also changed for the worse. Distinct periodicities of a Cheyne-Stokes type became apparent, with no stage of complete apnœa, but with a period of quite shallow respiration, lasting about sixty seconds and alternating with a deep snoring stage of shorter duration. Associated with this rhythmic alteration in respiration, changes in other activities were distinguishable, such as a rise in blood pressure of several millimetres, and great restlessness, both corresponding with the snoring period of respiration, and at the same time the eyes were apt to swing over to the left. A condition of ptosis of the left eye also developed. It was considered inadvisable to delay a craniotomy longer. Up to this time there had been nothing to evidence any particular localization of trouble. However, during the handling necessary for the preparation of the scalp the tender area over the right temporal bone was pressed upon, so that the patient winced, and in doing so moved the left side of the face much more than the right. Until this observation was made it had seemed a matter of indifference upon which side the craniotomy should be performed, inasmuch as the symptoms were believed to be due solely to a general increase in intracranial ten-

sion, as in Case II., rather than to any localized collection of blood. The evident facial paresis might have been resultant to one of two causes: either an implication of the peripheral neurons of the right nerve in the fracture of the temporal bone, or to a left-sided anæmia of the cortex brought about by the local compression of an extradural clot in that situation. This uncertainty, however, was sufficient to favor the turning down of a flap from the left side of the brain.

FIG. 2.

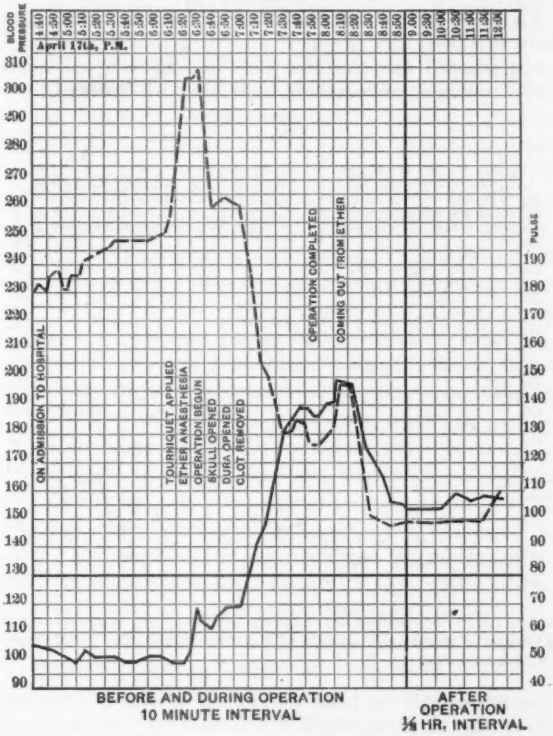


Chart of Case III. before, during, and immediately after operation. Broken line represents blood pressure in mm. of Hg. Solid line represents pulse rate.

That the surmise as to the probable location of the lesion causing this paralysis was a correct one, was shown by the fact that in the patient's struggles during the primary stage of anæsthesia there was evidence as well of considerable weakness in the right arm.

Operation, ether anæsthesia (one and a half hours after admission; two and one-half hours after reception of injury). As the blood-pressure chart shows, the application of the rubber tourniquet about the head and the administration of ether caused a great rise in arterial tension, namely, to 305 mm., almost an extreme level. It fell, however, nearly to its previous level before beginning the operation.

It is unnecessary here to go into full surgical details of the craniotomy. A large Wagner flap was turned down, its centre corresponding practically with the lower or facial portion of the cortical motor area. On elevating this flap a fissure was disclosed in the temporal bone crossing its entire extent, and passing down toward the base. Between the dura and the skull the upper edge of what was evidently a large blood clot was brought to view in the lower portion of the cerebral window. A further enlargement of the opening in a downward direction was necessary to satisfactorily expose it. This was rapidly done with Rongeur forceps, and a large clot, which had almost completely displaced the temporal lobe, was thus exposed. The clot was rapidly scooped out and the space it had occupied momentarily packed with gauze, as considerable fresh bleeding followed its removal.

FIG. 3.

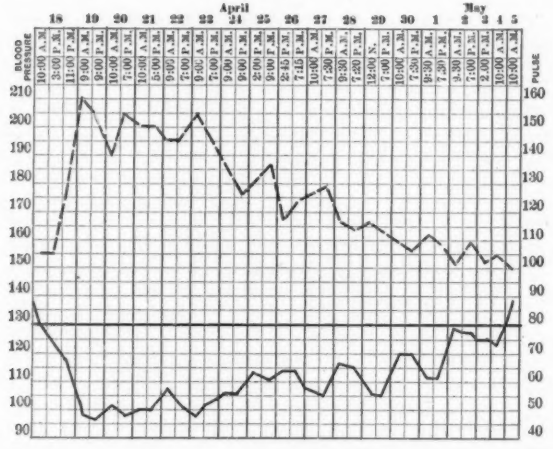


Chart of Case III. for the eighteen days after operation, showing post-operative evidence of secondary increase of intracranial tension, with gradual subsidence. Blood pressure, broken line; pulse rate, solid line.

The fissure through the bone could then be seen to run down across the base of the skull through the foramen spinosum, from which situation the bleeding was coming, probably from a ruptured middle meningeal artery.

The dura on first opening the skull was found to be very tense. It was opened, and an ounce of bloody cerebrospinal fluid under great tension was evacuated. It can be seen by consulting the blood-pressure chart (Fig. 2) that immediate relief was afforded to the extreme compression symptoms by the craniotomy and by the evacuation of the clot and superabundant subarachnoid fluid. The blood pressure returned to a safe level (150), and an accelerated pulse rate of from 130 to 140 momentarily took the place of the previous vagus pulse. Such an acceleration of the heart-beat is frequently seen in experimental conditions when there is a sudden release of the brain from

an increased tension which has previously produced vagus symptoms. The pulse soon slowed, however, and remained at 100.

The second chart (Fig. 3) shows the reaction during the period of convalescence and the gradual return to the normal of the increased blood pressure and slowed pulse, which on the day after the operation had once more shown a tendency to approach dangerous levels.

Discussion. I will not go into the details of the subsequent history of this case other than to say that the patient ultimately made a complete recovery. His condition cleared up very rapidly after the operation, although for some time he remained markedly aphasic. What is of interest for our present study, however, is the secondary rise in blood pressure and slowing of pulse shown in the chart (Fig. 3), which represents the average of the observations on pulse and blood pressure taken during the following two weeks. I can only explain this evidence of a secondary increase in intracranial tension, with its very gradual subsidence, by supposing, as in Case II. (Fig. 1), a condition of post-traumatic cerebral œdema of the Cannon-Bullard type. This relatively late reaction has been frequently seen in our traumatic brain cases.

The case is an unusual one from the rapid onset of the extreme symptoms of compression (Höhestadium des manifesten Hirndruckes). Here, again, was existent a combined process accounting for the increase in intracranial tension; on the one hand, an intermeningeal hemorrhage producing a certain general increase in intracranial tension much as in Case II., surmounted, on the other hand, by the local process consequent upon the extradural hemorrhage. This local process formed much more rapidly than is usual in case of extradural hemorrhage, probably owing to the fact that the meningeal artery was ruptured sufficiently low down to allow of a very rapid extravasation of blood. This hemorrhage in its upward progression, stripping away the dura from the skull, had finally reached and compressed the lower part of the motor cortex corresponding to facial movements at the time when the operation was commenced. Possibly either one of these two processes alone might not have sufficed to endanger the centres in the medulla. The two combined, however, produced a degree of compression which was rapidly approaching the "Lähmungsstadium" of the Germans. It is fortunate that relief could have been afforded so soon after the accident and before this stage set in. Operative intervention, when this third stage of compression is reached, is not always so gratifying in its results.

Examination of the Eye-grounds in States of Compression. It must be kept in mind that the underlying conditions which produce symptoms characterizing the various stages of compression are nothing more than degrees of interference with the normal intracranial circu-

lation, and that an increasing venous stasis is the first result of these circulatory disturbances. This, as has been pointed out elsewhere, may be readily appreciated during experimentally induced compression by the insertion in the skull of a close-fitting glass window through which alterations in the condition of vascularity of the exposed area of cortex may be observed, and in case the increase of tension is uniformly distributed ("general compression") these alterations may be taken as representative of the vascular conditions throughout the entire chamber. Fortunately, the ophthalmoscope offers a method of determining in clinical cases the presence or absence of intracranial venous stasis, inasmuch as the congestion is transmitted to and is easily observable in the veins of the fundus. Thus, the eye-grounds become almost equal in value to the experimental window. Unfortunately, however, during most of our operative procedures under anæsthesia the possibility of a continuous ophthalmoscopic examination is precluded, and although in several of our compression cases comparative examinations, before and after operative relief, have evidenced a diminution in the size of the veins in the eye-grounds this has never been seen at the exact time of its occurrence. An opportunity offered itself, however, on one occasion and under rather unusual circumstances which did allow an expert examination of the eye-grounds to be made at the very moment of giving relief to an advanced degree of intracranial tension. The patient on whom this examination was made was suffering from a pneumococcus posterior basic meningitis (Barlow), which had obstructed the foramina of the fourth ventricle and had led to an acute internal pyohydrocephalus. The increase of tension was such as to produce extreme symptoms of compression bordering on the terminal or paralytic stage. On several occasions the ventricles were tapped, and an ounce or two of seropurulent fluid evacuated with an immediate, though, unhappily, only a temporary amelioration of the symptoms, shown by a fall in blood pressure, an improvement in the pulse and respiration, and a considerable lessening of the mental stupor. These ventricular aspirations were easily performed without anæsthesia according to the method suggested by Albert Kocher for intraventricular injections, and during one of them Dr. Boardly followed closely with the ophthalmoscope the condition of the veins radiating toward the papilla. Immediately on removal of the ventricular fluid the veins, which had been tortuous and much engorged, became smaller in calibre, and lost much of their sinuous outline, while the arteries, on the other hand, became larger, more prominent, and seemingly more tortuous. Although I have frequently observed this change in dogs during the release of experimental compression, I am unaware that the observation has in so striking a fashion been made upon man. I think that too little stress is laid on the value of ophthalmoscopic examinations in the determination of

varying states of intracranial tension. Doubtless it is a difficult thing always to appreciate an increase in the size of the retinal veins, as they vary under normal conditions to such a considerable extent, but it should be possible with experience to recognize with some degree of probability the presence of this venous stasis, which plays such an important part even in the early stage of compression. It may be possible to gain this training by compressing the jugulars of patients on whom ophthalmoscopic examinations are being made. Dr. Boardly examined the writer's eye-grounds on one occasion while the inflatable band of a blood-pressure apparatus, which had been placed so as to encircle the neck, was gradually blown up. As soon as the recorded manometric pressure reached a level bordering on 80 mm. of Hg., an increase in size of the veins of the fundus became apparent. On a further increase of the pressure to 120 and 140 mm., or nearly to the level of arterial pressure, the veins increased in size fully one-third, and a sensation of dizziness, nausea, and stupor was experienced which quickly passed off on releasing the pressure. The venous stasis observable in the eye-grounds, of course, immediately disappeared.

CASE IV. (Surgical No. 14,081.) *Apoplexy with right hemiplegia; symptoms of pronounced intracranial tension evidenced by a blood pressure ranging about 300 mm. of Hg.; threatened symptoms of medullary paralysis; major symptoms (bulbar) immediately relieved by craniotomy and aspiration of intracerebral clot; Wagner flap left "ajar;" subsequent replacement of flap followed by return of symptoms; death on the third day from pulmonary complications.*—The patient, Frank W., colored, aged forty years, entered Dr. Halsted's service at 8 A.M. on November 23, 1902. On the evening of November 21st he was supposed to have fallen from a bicycle; was found in the street in a semiconscious condition, and was taken to the station-house as an inebriate.

At the time of his admission to the hospital, thirty-six hours after the onset of his symptoms, the following note was made on his condition:

"The patient lies in the dorsal position in a state of profound stupor, from which he can be aroused only in the slightest degree by the infliction of pain. There is an occasional aimless movement of the left arm or leg. The right side, with the exception of muscles supplied by the superior branch of the facial, is in a condition of complete paralytic flaccidity. His temperature registers 99.6°. The respiration varies in rate from 21 to 27. It is characterized by a distinct periodicity, a shallow and a stertorous, snoring period, alternating with considerable regularity. The pulse rate is regular, averaging 50 to the minute, and the arterial tension is very high. The blood pressure registers in the neighborhood of 300 mm. of Hg.

"Evidence of vasomotor rhythm is at times observable, the height of the blood-pressure wave corresponding with the period of deeper respirations, with restlessness and movements in the non-paralyzed side and with some pupillary dilatation.

"There is a persistent conjugate deviation of the eyes toward the right, associated with nystagmus. The pupils are equally contracted

and react to light. The veins of the forehead, median, and lateral are greatly distended.

"Reflexes: Deep reflexes readily obtained and are equal on both sides at the knee and ankle. They are not exaggerated. Superficial reflexes are abolished on the paralyzed side, plantar, cremasteric, and abdominal. They are present on the left. Visceral reflexes (sphincteric) are lost (?). McCarthy's reflex present on both sides.

"Anæsthesia, to painful stimuli at least, seems to be present on the paralyzed side. Some reflex response to pain can be obtained from the opposite side."

The history, such as could be obtained, indicated that the patient's stupor had been increasing, and in view of the great elevation in blood pressure and the beginning evidence of respiratory implication, it was determined to make an attempt to relieve the intracranial tension, and, if possible, to locate and evacuate the clot.

Operation, November 23d, 3 P.M. No anæsthesia required owing to deep stupor. A tourniquet was applied, and a large osteoplastic bone flap, measuring about 12 by 8 cm., was turned down from over the left hemisphere. Owing to the thickness of the negro's skull this performance, usually simple, was attended with some difficulty. The underlying dura was tense and without pulsation. On incising it, however, the brain bulged far into the opening, and began actively to pulsate. The convolutions were greatly flattened, deeply cyanosed, and the veins occupying the sulci were widely dilated and their contents so dark that the color contrast between veins and arteries was of an unusual degree.

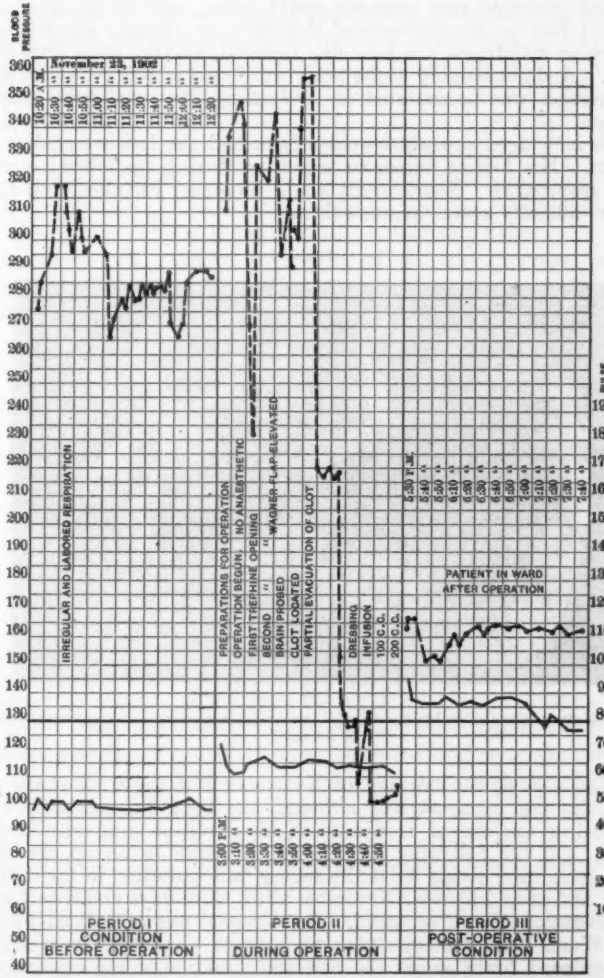
Through the convexity of one of the convolutions posterior to the fissure of Rolando a grooved director was passed into the substance of the brain in a slightly forward direction in the hope of tapping the site of hemorrhage. When the probe had entered a distance of 4 cm. a sudden lack of resistance was encountered as though it had entered a cavity, and dark, blackish fluid blood spurted out along the groove of the instrument. In the track of the director the handle of a scalpel, which was flat and had a sharp, rounded edge, was then introduced into the seat of hemorrhage. This was rewarded by the evacuation of about two teaspoonfuls of old, discolored, semifluid blood and clots. (A glance at the accompanying chart, Fig. 4, will show that the patient's blood pressure began abruptly to fall from its high level, approximately at 360 mm., and in the next twenty minutes had reached a normal level, there being, meanwhile, absolutely no change appreciable in pulse rate during this alteration in arterial tension, representing 230 mm. of Hg.)

The release from intracranial tension was evidenced by the immediate collapse of the bulging hemisphere. Two strips of rubber protective, to serve as drains, were passed into the cavity of the clot through the track which had been made. The bone flap was loosely replaced, no sutures whatever being taken in the skin. Strips of gauze were placed between the edges of the scalp and a loose gauze dressing over all. It was hoped in this way to allow for an elevation of the flap in safety-valve-like fashion, should there be once more a considerable increase in intracranial tension.

On November 24th, the day following the operative procedure, the patient's condition had greatly improved. The pulse rate and blood pressure remained within normal limits, his respiration was no longer

labored, his stupor was much less deep, and he could be aroused with considerable ease. He took nourishment by mouth for the first time since his "stroke," and at one time took a cup from the nurse's hand in order to drink himself. Slight voluntary movements of the right

FIG. 4.



Broken line, arterial tension; solid line, pulse rate. Three fragments of the blood-pressure chart of Case IV. Note in Period I. the high tension and slow pulse. In Period II. the release from the vasomotor overaction by the craniotomy and evacuation of clot. Fall of blood pressure of 260 mm. of Hg. without change in pulse rate. In Period III. the practically normal levels after operation.

arm were also present. The conjugate deviation of the pupils had disappeared, and he seemed to see and recognize objects. He would endeavor to protrude his tongue on request. There was no effort at speech (note that the lesion extended far forward in the left corona radiata) at any time.

Owing to the great amelioration in the gravity of symptoms, it was thought probable that recovery would ensue, and at an ill-advised moment late in the afternoon of this date the dressing was removed, the drains withdrawn, the bone flap replaced, and the scalp sutured in place. A slight bulging of the brain was found at this time, and some compression was necessitated in readjusting the osteoplastic flap in position.

This misjudged procedure evidently turned the balance against the patient. His former stuporous condition during the following night again reappeared. Nourishment could no longer be taken, and respiratory difficulty again became evident.

FIG. 5.

One of the sections of the brain of Case IV., showing the situation and transverse extent of the cavity

When seen on the morning of November 25th the error of the previous day was apparent, and although the bone flap was once more elevated in the hope of readjustment, his condition gradually became worse. On the following day the lungs began to fill up, the right heart gave way, giving a definite regurgitant pulsation in the cervical veins, and at midnight of November 27th, three days and a half after the operation, death occurred. An autopsy was performed by Dr. Van Wart. The accompanying photograph (Fig. 5) of a section of the hardened brain shows the size and situation of the hemorrhagic cavity. It was found practically empty.

DISCUSSION. Considerable interest attaches itself to this case and to a previous case of apoplexy (surgical No. 13,892) from Dr. Osler's

wards, in which an attempt was made in a similar way to ward off a fatal outcome by the elevation of a large osteoplastic flap. In this earlier case the patient's condition was much worse, and the stage of respiratory paralysis, at the time of operation, was seemingly near at hand. The symptomatic relief, nevertheless, was striking, and the blood pressure fell immediately after opening the dura to an approximately normal level, at which it remained until death ensued from pulmonary complications, thirty-six hours later. The seat of hemorrhage in this earlier case, unfortunately, had not been sought for with sufficient freedom, and at autopsy a large clot the size of a hen's egg was found closely underlying the cortex and in exact correspondence with the opening in the skull. Had it been located and the cortex been freely incised the clot under great tension probably would have been forcibly extruded by the pressure of the surrounding brain.

The propriety of surgical procedures of this sort doubtless will be questioned by many, and I believe that only in exceptional cases will surgical measures hold out any prospect of success, and then only when the interpretations of blood-pressure observations are utilized as an indication for the necessity of intervention, as well as a means of estimating the degree of vascular relief gained by the trepanation. I am unaware that the attempt has heretofore been made with any rational intent to bring relief to the cases of extensive hemorrhage spreading from the capsule into the corona radiata, and I do not see any reason why we should exclude these cases from possibilities of surgical relief simply because the hemorrhage lies beneath the cortex, any more than that intracranial hemorrhage in other situations should be allowed to run its course. The majority of the cases of apoplexy which are exposed on the autopsy table show a large clot more or less readily accessible to operative attack, and one would be much chagrined to have an extradural hemorrhage of corresponding size brought to light post-mortem without an attempt having been made to remove it by operation. The underlying or major symptoms of compression are the same whether the collection of blood be extradural or within the substance of the brain itself. Whether the extravasated blood in apoplexy is in most instances rapidly coagulated or not can hardly be known until more cases have been explored before death, but it is presumable that it is and not improbable that the release of intracranial tension from the elevation of the bone flap, and especially from the evacuation of the clot, should one have been located, will, by the consequent rapid lowering of blood pressure, tend to check any further hemorrhage, even in case the ruptured artery should not previously have ceased to bleed.

The therapeutic measure generally advocated in case of intracranial hemorrhage with high-bounding pulse is a purely symptomatic one,

namely, "to bleed" the patient in order to lower blood pressure, the idea being that the persistent high tension is the cause rather than the result of the hemorrhage. If the interpretation of the experimental work is not at fault such an abstraction of blood with the idea of lowering arterial tension would be absolutely contraindicated, since the high blood pressure is only an indication of nature's effort to overcome the degree of intracranial pressure brought about by the foreign body in order to ward off an anæmic condition of the bulbar centres. Of course, the tension of the foreign body in this case, communicating as it does with a ruptured artery, is equal to that of the arterial tension, and were it not for its remoteness, ordinarily, from the medulla, death would almost immediately ensue, just as it does when a hemorrhage takes place in the near neighborhood of the medulla or reaches the fourth ventricle through rupture into one of the lateral ventricular cavities.

In the course of many of the experiments on compression the effects of blood-letting (the skull still being intact) were tried during the various stages of compression. At no time could any beneficial influences be seen, and if blood were withdrawn from the general circulation at a time when there had been a marked rise in general arterial tension to overcome cerebral anæmia, and in amounts sufficient to lower this vascular tension, the results were almost always disastrous unless a certain amount of reserve power remained in the vasomotor centre which could once more return the arterial tension to its former level. I would not mean to deny that symptomatic improvement ever follows blood-letting in cases of apoplexy in which the hemorrhages have not called forth pronounced symptoms referable to the vital bulbar centres, but when such is the case anything which tends to lower arterial tension without an associated opening in the skull to correspondingly lower intracranial tension is hazardous to say the least.

In dismissing these cases of apoplexy, representing as they do extreme types of the advanced stage of compression, it may be said that despite the ultimate failure of recovery in these two unfavorable cases, the temporary amelioration of the severe symptoms is a sufficient justification for future attempts to afford surgical relief to certain carefully selected cases of cerebral hemorrhage.[1]

CASE V. *Penetrating gunshot wound of skull; intracerebral hemorrhage; paralysis stage of compression with vasomotor and subsequent*

[1] Since writing the above note concerning the possibility of operative attack in apoplectic cases a patient has been in the hospital, under the care of Dr. Thomas and myself, in whom a subcortical hemorrhage had formed as the result of a stab wound of the cranial vault. A craniotomy was performed in this case; the clot was exposed, evacuated, and its cavity irrigated with salt solution; the bone flap was replaced, and the patient made a rapid and almost total recovery from the symptoms which the hemorrhage had caused. As in the case of apoplexy above recorded, the clot almost extruded itself through the opening made in the brain substance to reach it. Others have reported cases of recovery after operation for subcortical hemorrhages of traumatic origin.

respiratory failure; craniotomy during artificial respiration; long continuance of heart-beat; exitus.—The patient, a young woman, aged eighteen years, was brought to the hospital about 3 P.M. on April 21, 1902, soon after the reception of her injury. When seen in the accident room immediately after her admission it was recognized that she was almost in the "Lähmungsstadium" of compression, and rapid preparations were made for operation.

The only history obtainable was to the effect that she had been shot by her husband about one hour before admission. Examination showed that the bullet had penetrated the squamous portion of the right temporal bone, nearly 5 cm. above the zygomatic arch. Cerebral substance was protruding from and being squeezed through the wound; an invariable sequence of great increase in intracranial tension, when associated with a small opening through the skull and dura, which leaves the underlying brain unsupported. There was no wound of exit.

The patient was in deep coma. Her respirations were slow, gasping, and irregular, with periods of apnœa. The pulse was rapid, 160, of irregular rhythm, and the arterial tension was low. Blood-pressure observations, which were immediately instituted, demonstrated that a very rapid fall was taking place. The eyes were fixed, staring, and prominent, with widely and equally dilated pupils. The face was much cyanosed, and ecchymoses were already forming in the eyelids and conjunctivæ. She vomited soon after her admission, in projectile fashion.

It was apparent that she was advanced in pregnancy. Owing to the urgency of the case, further examination was not made, and the patient was hurried to the adjoining operating-room. On the way thither the respirations, which, in the few moments intervening since her entrance, had become much more irregular in character, ceased altogether. Artificial respiration, by thoracic compression, was kept up, until the patient could be put upon the table, when a rapid tracheotomy was performed, and a tube inserted in the trachea. After a moment of mouth-to-tube inflation, the color quickly returned to the deeply cyanosed face, and the pulse, which had continued during this interval, greatly improved in character.

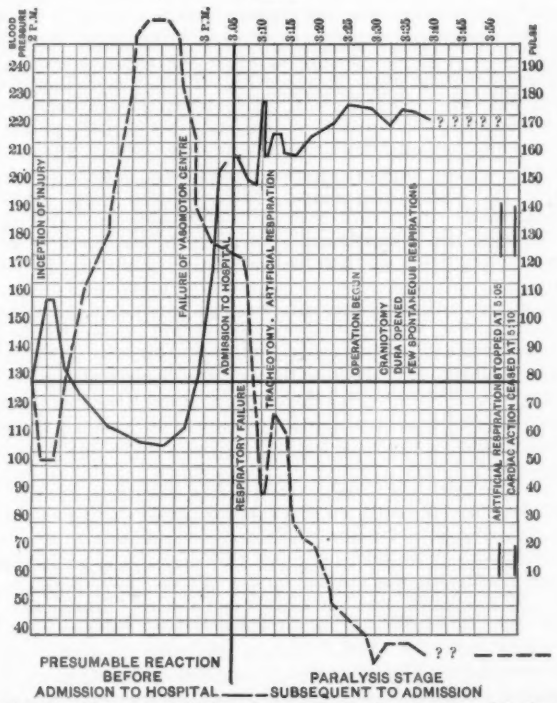
Meanwhile, an extensive area from the side of the scalp was being shaved; a tourniquet was applied, and a Wagner bone flap, the size of the palm of the hand, was quickly turned down.[1] There was a vain hope that the vasomotor and respiratory failure did not evidence an irrecoverable paralysis of the centres, and that prompt relief from anæmia, due to the extreme degree of intracranial tension, would allow of medullary circulation, sufficient to reawaken the centres to activity.

With three lives at stake—that of the assailant, his victim, and a child—the moments consumed during this partial hemicraniotomy under artificial respiration were exciting enough, and we were rewarded,

[1] In the absence of a motor with a burr and a Doyen saw a comparatively rapid way of making such a flap is to penetrate the skull with trephine or mallet and gouge in two places corresponding to the angles at the superior base line of the proposed flap. These openings may in a moment be rapidly connected with a Gigli saw and the two lateral edges cut out rapidly with the de Vilbiss forceps. Twelve minutes should suffice by this procedure for a safe exposure of a wide area of dura. A tourniquet should always be applied about the base of the cranium to control hemorrhage from the scalp during the procedure. This otherwise occasions much delay.

after the final opening of skull and dura, by the patient's taking, for the first time, a few spontaneous gasping inspirations. The hemisphere bulged under considerable tension from the opening, and a large amount of blood clot was evacuated. To our great disappointment, the voluntary efforts at respiration did not long continue, and it was once more necessary to resort to artificial means of continuing it. The blood pressure, meanwhile, had been steadily and rapidly falling (see chart, Fig. 6), until it had reached its level of complete vasomotor paralysis, representing only 20 to 30 mm. of Hg.—a condition from

FIG. 6.



Broken line, blood pressure; solid line, pulse rate. Blood-pressure record in Case V. Presumable reaction from the time of injury to death, two hours later. First portion of chart hypothetical.

which there is probably no recovery. The heart, however, like the isolated mammalian heart of the physiological experiment, continued to beat as long as its circulating blood was kept aërated by the continuance of artificial respiration. As long as there is cardiac pulsation, it is difficult to bring one's self to a realization of the actual presence of death, and artificial breathing was continued for two hours longer before its final abandonment.

Had the child been at or near full term, during the two hours and a

half of artificial respiration a Cæsarean section might, at any time, have saved it. During the craniotomy, however, the woman was examined by a member of the obstetrical staff, who pronounced the infant too premature to justify the procedure. On cessation of the artificial respiration, the patient became progressively more and more cyanosed, the heart-beat soon weakened, and, after two or three minutes, could no longer be auscultated.

Discussion. This case is cited not only as typifying the sequence of events in the so-called paralysis stage of compression, but also as an indication of what may be accomplished in rare instances under similar desperate circumstances. The accompanying chart (Fig. 6) records the observations which were actually taken after the patient's admission to the hospital, and also gives the reaction which by analogy with experimental conditions can be imagined to have taken place during the hour preceding, viz., a slowing of pulse and a great rise in blood pressure, which anticipated the failure of the vasomotor centre and resultant respiratory paralysis. Under just such circumstances in animal experimentation when intracranial tension has been increased so as to exceed the level to which arterial tension can be forced, or when the latter has been held at a high level long enough to bring about fatigue of the vasomotor centre, the life of the animal may be saved by the establishment of artificial respiration and a hurried release from the compressing force. It is impossible to say for how long a time a compression anæmia of the medulla in man may persist and still leave the respiratory and vasomotor centres in a recoverable condition. There can be no doubt, however, as evidenced by some cases which have been reported, that life may be prolonged by artificial respiration for a length of time at least sufficient to allow of operative relief from the compression. Every effort should be made after the craniotomy to restore once more the vasomotor tone, in case the simple release from pressure is not sufficient. Ordinary stimulants will not suffice for this, and it is to be hoped that when the therapeutic indications of adrenalin are finally laid down that it may prove to be the drug which can be depended upon to restore activity to cerebral centres which have suffered exhaustion from long-standing anæmia. In case hemorrhage is not under absolute control the administration of adrenalin is attended with risks, as the following incident will illustrate:

A patient was recently admitted to the hospital with a penetrating bullet wound of the brain, and very soon after admission, and while preparations were being made for operation, he passed into the "Lähmungsstadium" of compression, due to intracranial hemorrhage. Dr. Tinker performed a rapid craniotomy, which, as in the case reported above, did not suffice, through the release from pressure, to reawaken the activity of the vital centres. The blood pressure had fallen to its paralysis level, and artificial respiration had to be resorted to. Intra-

venous injections of a weak adrenalin-chloride solution were administered as a last resort, and, although the blood pressure could be held at any desired level during the infusion, the improved circulation did not suffice to restore activity in the paralyzed centres. The rise in blood pressure did nothing more than renew the bleeding from the wound in the bulging brain, and, on discontinuing the infusion, the pressure immediately fell to its pre-existing or even to a lower level. As in profound shock, so here, there seems to be an exhaustion of the vasomotor centre from overaction, which in the former state is brought about by reflex sensory stimulation, in the latter by direct stimulation of the centre from anæmia. The result in both instances is a profound and enduring drop in blood pressure, and, ordinarily, therapy is impotent to restore activity to the centre.

Isolated reports are to be found of procedures similar to that recorded above and carried out under artificial respiration in which there has been a successful re-establishment of voluntary respiration. These have been cases, I believe, almost without exception in which a cerebral abscess has been the cause of the increased tension and resultant medullary anæmia, and the prompt evacuation of pus has allowed a sufficient readjustment of circulatory conditions to reawaken the centres in the bulb.

Sir Victor Horsley[1] has called especial attention to the early respiratory failure under these circumstances, and has emphasized the fact that these cases "die from failure of respiration, and not, as is so often surmised, from failure of the heart."

The practical point which Horsley establishes in his communication is that there is a continuance of cardiac action after the respiratory failure, and consequently artificial respiration may suffice to prolong life in favorable cases until a craniotomy can be performed and the pressure relieved. In one of his cases respiratory failure, as in the case above reported, occurred on the operating-table; the skull was immediately opened, the brain bulged, the pressure was relieved, normal respiration was re-established, and the patient recovered.

It seems possible to retrace the sequence of paralyses of the centres one step farther than Horsley has gone, and to explain the supposed primary respiratory failure by a preceding vasomotor failure. Horsley and Spencer supposed that the medullary paralyses were produced by the mere mechanical effect of pressure exerted on the centres. Leonard Hill, however, in his classical monograph, gives experimental proof to show that it is rather the state of vascular anæmia which paralyzes the centres, and with this our experiments are in accord. Hill, however, does not mention the regulatory action of the vasomotor

[1] On the Mode of Death in Cerebral Compression, and its Prevention. Quarterly Medical Journal, July, 1894, vol. ii. p. 305.

centre which serves to ward off the condition of threatened anæmia by an elevation of blood pressure. The possibility of long continuance of cardiac action after primary vasomotor and secondary respiratory failure was shown by a case reported in the Mütter lecture,[1] in which under artificial respiration the heart-beat continued for twenty-three hours. Spencer[2] has recorded similar cases in which the heart-beat continued twenty-four, six, and eight and one-half hours after cessation of voluntary breathing. Macewen, likewise, in his well-known volume,[3] mentions other instances, in one of which breathing was re-established after some hours of artificial respiration. Hudson[4] has more recently added additional cases of the same sort.

To reiterate: After fatigue or failure of the vasomotor centre the blood pressure falls to a point below that of the intracranial or extravascular tension; anæmia consequently ensues; respiration, already embarrassed at this point, immediately ceases from total lack of vascularization of the centre, and unless relief is given the blood pressure gradually sinks to a level which represents irrecoverable paralysis of the centre governing it. Even when this has occurred artificial respiration with proper aëration of the blood may suffice to keep the individual's heart beating for hours.

In briefly summarizing the subjects of discussion in this paper, attention may be again drawn to the following points:

Varying degrees of rapid increase in intracranial tension produce corresponding disturbances in the intracranial circulation. To these circulatory disturbances the symptoms of compression are solely due. The condition known as acute cerebral compression may be conveniently subdivided into four stages, dependent upon the degree of circulatory alteration which has been reached. Each of the stages has its own more or less characteristic symptom-complex.

The major or underlying symptoms originate in the centres situated in the medulla, and are only called out when the degree of intracranial tension begins to approach the arterial tension so that anæmia is threatened. A circulatory condition in the medulla which borders upon anæmia has the effect of stimulating the vasomotor centre. Thus, a rise in blood pressure is occasioned which restores the local circulation. The extent of this rise may be taken as an indication of the degree of advancement of the compression. Beyond a certain point, however, this reaction cannot take place. The vasomotor centre

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1902, vol. cxxiv. p. 393.

[2] The Arris and Gale Lectures on the Central Nervous Mechanism of the Respiration. The Lancet, March 2, 1895, p. 533.

[3] Pyogenic Diseases of the Brain and Spinal Cord. Glasgow, 1893, p. 136.

[4] Respiratory Failure Occurring Before Circulatory Failure in Brain Injury and Disease. Medical News, June 10, 1899.

under these circumstances fails, and the respiratory efforts cease entirely.

In conjunction with other symptoms, a progressive increase in arterial pressure or a high degree of the same, which has been already reached, or a pressure which exhibits from moment to moment great alterations in level may be taken as a certain indication of the advisability of early operative intervention. In case there are localizable symptoms the site of trepanation is plainly indicated. In case of generalized compression from widespread hemorrhage when there are no localizing indications, the intracranial tension should be relieved by the elevation of a large osteoplastic flap from one hemisphere or the other with a corresponding opening in the dura.

A REVIEW OF SOME OF THE OLDER WRITINGS ON INFANT FEEDING.*

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It was my original intention to embody in this paper a review of the literature relating to maternal nursing, but this idea was abandoned when it was once realized how much there was to consider under substitute feeding. The gist of everything that has been written on maternal nursing can be summed up in a few words: All authorities in the past two centuries have advised mother's milk as preferable to all other forms of infant diet. Prior to this time, however, according to Van Swieten (Paul's translation, 1759), Van Helmont and his school opposed milk in any form.

Substitute Feeding. That much has been written on substitute feeding goes without saying. To do justice to all of it is obviously impossible. My comments, therefore, will be limited chiefly to the writings of the eighteenth century, which were at my disposal, and to the most interesting and important of the works of the first half of the past century, considering only a few of those which have appeared since that time. In doing this I will quote freely from those authors who have written interestingly and instructively.

The methods which have been in favor are three in number: (1) wet-nursing; (2) direct nursing from animals, and (3) the use of artificially prepared foods. All of the older writers are in accord in

* Read before the Section on Pediatrics of the New York Academy of Medicine, October 9, 1902.

preferring the first of these—*the wet-nurse*—although this measure has never been considered in any sense comparable to maternal feeding.

It has been impossible to fix upon the date of the beginning of wet-nursing as a common practice. It is probably safe to assume that it has been indulged in to some extent in all times. It has been a very prevalent custom in the times of which I write, and at certain periods was evidently practised to an extreme degree. John Clarke, writing in London in 1815, says that "The prevalent custom of relegating all children to wet-nursing or dry-nursing has resulted in reducing the supply of wet-nurses and in inducing the wet-nurse to forsake her own child, which invariably dies; therefore, it is hardly a question whether society at large is a gainer or loser by the employment of hired wet-nurses." The moral aspect of the wet-nurse question was evidently more commonly considered formerly than now. "This custom," Clarke goes on to say, "acts as a further detriment to society in that it leads to the neglect of older children, lack of attention to household duties, dissatisfaction with home surroundings, and consequent family differences." He thought that, "On the whole, it would be better perhaps that the children of the wealthy should be brought up artificially where the mother does not suckle them, because they would have every advantage of good nursing, cleanliness, air, and medical treatment, and would, therefore, have a better chance of living than the child of the wet-nurse." He suggested another plan to relieve the difficulty, namely, to have a vigorous wet-nurse feed both her own and the foster-child, the deficiency being made up artificially. John Roberton (London, 1807) refers to the same evils pointed out by Clarke, and suggests much the same remedies. He likewise considered it "the duty of the professional man to make the unfortunate infant deprived of its natural source of feeding every amends in his power."

Dewees (1825) preferred the sucking bottle to "the hireling nurse," unless it be known that the nurse is a person "capable in every respect of fulfilling the important duty of suckling." He pointed out that "the withdrawal of the wet-nurse from her own child and family, in benefiting one part of society, injured another." In order to obviate this, he suggested "that only those women who have lost their own children be employed." He was opposed to their nursing both their own and the foster-child, lest the latter receive too little nourishment.

The following rules laid down by Van Swieten as early as 1759 for the selection of a wet-nurse are most comprehensive and have not been much improved: "She should be examined by a physician, who should determine that she has perfect health; that her skin is natural in color, her eyes lively and animated, her gums firm and of good color, her teeth healthy and clean, her lips red, her habits of body neat and clean, and that no odor exhale from her mouth or nose or any other

part. He should also determine that her own child is well nourished." Beside "a prudent monthly nurse should examine every part of her body to exclude suspicious scars or pimples." "She should be from twenty-five to thirty years old, and it is best that she should have borne several children. Her breasts should be firm, distended, elastic, and of medium size." "Large breasts furnish little milk," and, according to Aetius, "in large breasts much swollen with the quantity of milk it becomes corrupted by remaining there, and consequently noxious to the child." "The nipple should be red, firm, and large, but not so large as to interfere with the freedom of the tongue's movements. The milk should run easily and spout a good distance like so many little siphons when the breast is pressed."

Rosen von Rosenstein (1776) indorsed the following lines from St. Marthe's *Pædotrophia* (Tytler's translation) as covering all the points necessary to be considered in the selection of a wet-nurse:

"Choose one of middle age, nor old nor young,
Nor plump nor slim her make, but firm and strong.
Upon her cheek let health refulgent glow
In vivid colors that good humor show.
Long be her arms and broad her ample chest,
Her neck be finely turned and full her breast.
Let the twin hills be white as mountain snow,
Their swelling veins with circling juices flow,
Each in a well-projecting nipple end,
And milk in copious streams from these descend.
Remember too the whitish milk you meet
Of grateful flavor, pleasing taste and sweet
Is always best; and if it strongly scent
The air, some latent ill the vessels vent."

The securing of a satisfactory wet-nurse is not a purely modern difficulty. George Armstrong (1783) found that "a good wet-nurse is not always to be had, especially in or near great cities, where so many of them are given to drinking and other vices, and the worst of them will fall upon means of securing a good character." He found that the tendency on the part of the wealthy to indulge wet-nurses in all directions, especially in the giving of large salaries, "led to the ruination of many, making them as a class very unreliable." Clarke and many others refer to this, and several of the writers in the early part of the nineteenth century advised "that nurses owing to their loose morals be carefully guarded and deprived of all care of the infant, seeing it only at the time of nursing."

Direct Nursing from Animals. The second method of substitute feeding is one which has never come into common usage for several reasons: First, it has many repellent features; second, the milk of animals is not adapted to the digestive powers of infants; third, the method is not practicable. The goat, sheep, ass, and cow, the animals that have been in favor for this purpose, are not convenient household

pets, especially in our cities. Several of the earlier writers refer to the custom, and one or two practised it. Chambon (1799), for instance, preferred "suckling infants directly from a goat, a sheep, or an ass, to any form of substitute feeding." "The first," he found "very easy to manage, as goats proved susceptible to an attachment for the children which they nursed." He says "they come when full into the house and place themselves in a comfortable position to give the udder to the nursling."

At a much later period (1840) Andrew Combe quotes Dr. Von Ammon as advising that at the fifth month "the child should drain his food directly from the cow, and thus receive it in its natural state and at its natural temperature," and in support of his recommendation he says "infants fed in this way in the country thrive far better than those fed on cow's milk in towns."

Even at the present day in some parts of France infants are nursed directly from cows, and sometimes with good results. It is very probable that in Spain and Italy, where goats are commonly used as a source of milk supply, direct nursing is indulged in. Dr. Rotch (*Pediatrics*) refers to having observed a family of eight children "all of whom were nursed by the family cow, and were all healthy and strong."

It has usually been customary, however, when wet-nursing was impossible, to resort to some one of the various methods of artificial feeding.

Artificial Feeding. The foods which have been in most common use for this purpose are the milk of the ass, the goat, and the cow, broths made from the flesh of animals, and an innumerable variety of starch-containing and mucilaginous decoctions. The milk of the ass and the goat is still extensively used in some countries, and at one time was pretty generally preferred to that of the cow. It was early recognized, however, that the difficulty in securing the milk of these animals rendered this source of food impracticable. For this reason, the milk of the cow has been much more generally used. The milk of the ass and the goat, owing to its greater similarity to human milk, was usually given undiluted. The milk of the cow, on the other hand, has been given in a diluted form for many years. Judson and Gittings, in their recent work on *The Artificial Feeding of Infants* (Philadelphia, 1902), state that "the necessity of dilution to adapt cow's milk to the infant's powers of digestion was recognized as far back as the middle of the eighteenth century." They quote from the work of J. P. Frank, *On the Raising of Healthy Infants* (1749), to the effect that "Van Swieten, Loseke, and Cosner were the first to recommend diluted cow's milk for infant feeding; they advised to dilute from two to five times with water."

I have not had access to the writings of Loseke and Cosner to confirm Frank's observation respecting their methods, but in Paul's translation

of the *Aphorisms of Boerhaave*, with comments by Van Swieten, I find no reference to diluted cow's milk. It would not be surprising, however, to find that Van Swieten made some such recommendation, since his writings show evidence of an advanced and thoughtful mind. In some works of earlier date than this—the work of Walter Harris (1742) for instance—one fails to find any reference to the subject. Some of them do not even mention cow's milk, advising instead the milk of the ass or goat or some one of the various paps or panadas. Van Swieten quotes Von Helmont—who wrote in the very early part of the eighteenth century—as condemning the use of milk of all kinds, his objection being that "milk turns sour in the stomach." He preferred "a pap made with beer," which Van Swieten considered "a very singular preference which he did not satisfactorily explain."

The earliest reference I could find to the use of diluted cow's milk was in Sparrman's translation of Nicholas Rosen von Rosenstein's *Diseases of Children and Their Remedies*, published in 1776. He advised the use of "cow's or goat's milk—unboiled—diluted with water and sweetened with a little sugar." He sometimes used barley-water as a diluent, and where constipation existed he added a little thin filtered oatmeal gruel in which there had been dissolved a little clarified honey. He objected to the use of paps as "too gluey, tenacious and slimy and liable to produce obstructions in the mesentery, hardness of the stomach, acidities, wind, etc., by means of which we lose at least the one-half of our children." At the age of six months he gave whole milk containing rye biscuit which had been previously soaked in water. He fails to specify the amount of his dilution.

Underwood (1789) used somewhat similar but equally indefinite dilutions. He preferred either "water in which a piece of roll and some upper crust had been boiled, or hartshorn shavings boiled in water to the consistence that veal broth acquired when cold" as his diluent. To this mixture he added a little Lisbon or loaf-sugar. He, like Rosen von Rosenstein, was opposed to the use of paps and panadas in early infancy, but toward the end of the first year he gave some bread panada with broth.

George Armstrong, writing a few years earlier (1783), who considered himself well qualified to advise upon the subject of dry-nursing, in "that he had had some experience of it in his own family," directed as an adjuvant to maternal nursing "crumb of stale bread or, preferably, roll boiled in soft water to the consistency of pap, sweetened with a little soft or Lisbon sugar." For hand-fed infants, however, he directed that "cow's milk be added to their victuals as often as possible, and now and then some of it alone to drink." After weaning he used, in addition to other foods, "water in which the upper crust of bread had been boiled, mixed with an equal quantity of new

or boiled milk." This is the first instance in which the proportions of milk and water are indicated. It is probably safe to assume that the cow's milk used by this author as an adjuvant to maternal nursing, although not so stated, was a diluted milk. It is not probable that he would reserve the diluted milk for the latter months of the first year.

Moss (1794) gave much more definite directions for the modification of milk than did any of his predecessors. His ideas were advanced, instructive, and clearly expressed. He wrote thus: "Owing to trouble in the mother and inability to get a wet-nurse, it is sometimes necessary to secure some artificial food, for which purpose it will be advisable and proper to make choice of such food as appears to approach the nearest in quality to mother's milk. Ass's milk comes nearest to the human of any we are acquainted with, and, therefore, when it can be had it is very desirable and proper. Cow's milk being the only milk in general use, must be had recourse to, and will answer the purpose very well; but as it is a good bit thicker than breast milk, it will be necessary to reduce it to the proper consistence by diluting it with water. If the milk be good, about one part milk and two parts water will do very well to give at first. It is always best to err on the side of too great dilution." This mixture, which represents the same dilution as that advocated by the elder Meigs in 1850, was indirectly dependent upon some chemical analyses of cow's and human milk made by one Hoffman. This experimenter found that the inspissated residue obtained by the evaporation of cow's and human milk was as 13 to 8. On this basis Moss attempted the production of an artificial human milk by the dilution of cow's milk with water in the same proportion. This mixture seeming to the sight and taste so much stronger than human milk, he gradually increased the dilution until he obtained a mixture "possessing as nearly as possible the physical properties of human milk." His 1 in 3 mixture was the result; but even this, he says, "seemed a little less dilute than human milk." He did not consider the addition of sugar necessary unless the infant had been used to sweetened food. In preparing this food he used the freshest milk possible, preferring that just from the cow. He mixed at one time only enough to serve for a single feeding. This mixture he found could be advantageously substituted for mother's milk, and that "in general it agreed with infants much better than the other kinds of foods with which they were usually fed."

He was opposed to boiling, believing that this "made milk harder of digestion and binding; warming without boiling also did this, but to a less degree." In addition to milk he gave "chicken or veal tea to children who were dry-nursed," preferring the latter for the following very amusing reason: "It seems highly probable that the juices of

the young of those animals that feed upon milk are more likely to prove acceptable to the stomach of a child than those of the animals, as the cow, that may have formerly fed upon milk. The juices of the young sucking animals must be considered in a state approaching nearer to milk than those of other animals that do not derive their support from milk. Their juices, as partially abstracted by slight boiling, appear to be no other than milk somewhat more elaborated, assimilated, and animalized."

Struve (1801) used an equal quantity of milk and water in the preparation of a pap which he recommended. He considered the most wholesome beverage for children during dentition to be "equal parts of milk and water;" but when dry-nursing was first begun he advised "two-thirds of water to one of milk." "This should not be boiled, but heated to the boiling-point." He also highly recommended sweet whey prepared according to the following formula (Hufeland): "A slice of calf's stomach which had been prepared in vinegar and dried, should be soaked for two hours in a cup of water and then poured with the water into a pot of unboiled milk, from which the cream has been carefully separated. This is gradually heated, but not boiled. After a quarter of an hour the cheesy portion separates and the whey is left below. This should be poured off from the curds." He found that in the first months infants could live upon this alone.

Chambon (1799) used a mixture similar to that prescribed by Struve, but he preferred a preparation of grated crust of bread boiled in cream.

Heberden (1807) considered the object aimed at in artificial feeding to be the preparation of a mixture that resembles the mother's milk as nearly as possible. To accomplish this he used "ass's milk or milk and water with a little sugar of milk mixed with a little gruel, barley water, thin panada, or rice water, passed through a lawn sieve to insure their being smooth."

Roberton (1807), writing in the same year, found cow's milk objectionable at an early age on account of the large proportion of its curd; but cream diluted with five or six parts of water he used advantageously. He gave the preference, however, to "biscuit powder or small crackers boiled in water to a thin gruel, carefully beaten through a sieve and sweetened with fine sugar."

James Hamilton (1809) preferred "ass's milk or cow's milk mixed with a little water and sugar to which a small portion of milk biscuit may be added." He also used "arrowroot or patent sago mixed with water and milk, and to a less degree pap and panada." He added weak beef or chicken tea occasionally after the third month.

John Clarke, London (1815), whose work is very instructive and interesting, advised an "entirely fluid diet" that should be taken until the teeth appear. For this purpose he used ass's milk or "cow's milk pre-

viously skimmed, with two-thirds or three-fourths of its measure of gruel made from pearl barley, grits, rice, or arrowroot." "Where so mixed," he says, "the curd does not become so hard in the stomach as when diluted with water alone." As the child grew older the proportion of milk was gradually increased. Where this mixture disagreed he gave weak mutton, chicken, or beef broth, "clear and free from fat, mixed with an equal measure of any of the mucilaginous or farinaceous decoctions." After the appearance of the teeth he gave solid farinaceous substances boiled in water, beaten through a sieve and mixed with a small quantity of milk.

In instances in which the above preparations disagreed he sometimes obtained good results from a mixture of the farinaceous decoctions with a little cream.

Judson and Gittings, on the basis of this last suggestion, refer to Clarke as "one of the first to advocate the employment of cream diluted with starchy decoctions." As has been previously pointed out, Chambon, in 1799, recommended as useful a mixture composed of grated crust of bread dissolved in cream. His purpose in using this preparation—its "slight susceptibility to acid fermentation in the stomach"—was not the same as Clarke's. The latter added the starches for the same reason that they are often used to-day, namely, to break up the thicker curd of cow's milk. When so mixed, he says "the curd does not become as hard in the stomach as when diluted in water alone." So while their practices were much the same, and their results probably akin, the principles on which these results were based were entirely apart.

Dewees (1825), whose work seems to have been closely followed by other writers for many years, advised a mixture composed of milk two-thirds, water one-third, and "a small quantity of loaf-sugar." He used pure home milk as fresh as possible and from one cow. He gave very explicit directions regarding the preparation and care of his milk mixture. He advised that each feeding be prepared separately, that it be heated by the addition of hot water or on the sand-bath, and that the milk be kept in a cool place, and when in the least acid, rejected. Milk should never be boiled. In hot weather "it is true the tendency to decomposition is diminished by boiling; but this can be as satisfactorily accomplished by putting it, closely covered, over a hot fire and bringing it to the boiling-point; so soon as this is reached it should be removed and cooled as speedily as possible." "This plan prevents in a great degree the formation of the strong pellicle on the top, which deprives the milk of a portion of one of its most valuable parts."

James Kennedy (Glasgow, 1825), writing in Scotland in the same year, advocated what is, as far as I can ascertain, the first cream and whey mixture. He says "such forms of prepared aliment are preferable,

as they consist of milky and farinaceous substances agreeably sweetened. Of all these, recent cream of cow's milk diluted with whey (made from rennet) and arrowroot appear, from experience, to be the most congenial." He did not specify the proportions of the different ingredients used.

During the fourth decade of the nineteenth century little new was added to the methods of infant feeding. Practically all of the writers, as has been intimated, adopted the recommendations of Dewees. Marshall Hall (1831) preferred "pure beef tea without spice and with or without sago" to any of the milk foods. Eberle (1833) advised "farinaceous decoctions mixed with a small portion of cream" where no other form of milk could be given, and Combe (1840) advocated "fresh cow's milk, tepid and diluted with half or more of water and slightly sweetened." Cow's milk given in this way he considered "decidedly preferable to gruel, panada, arrowroot, chicken tea, or any other preparation less analogous to the natural food of the child." When children were artificially fed from birth the first food he suggested was composed of "two-thirds of pure fresh water added to one-third cow's milk. Goat's or ass's milk does not require more than an equal quantity of water." "After a week or two the water may be reduced to one-half, and later to one-third, at which proportion it should be continued for four or five months." This dilution, it is noted, is greater than that recommended by Dewees and his successors, and the attempt is here made to gradually increase the strength of the mixture as the age advances. Combe urged the utmost cleanliness regarding the care of dairy implements, and considered the excellence of dairy products in "Holland and other places" as "due almost entirely to this single cause."

It was not until the elder Meigs, in the second edition of his work on *The Diseases of Children* (1853), published his revolutionizing formula that the subject of infant feeding received a new and much-needed impetus.

Meigs was the first writer to appreciate the necessity of adding cream in order to obtain a proper fat percentage in his mixture. The mixture known for so many years by his name was prepared as follows: "A scruple of gelatin was soaked for a short time in eight tablespoonfuls of cold water and then boiled until it was dissolved, for about ten or fifteen minutes. To this was added, with constant stirring and just at the termination of the boiling, one-half pint of milk and arrowroot, the latter being previously mixed into a paste with a little cold water. After the addition of the milk or arrowroot and just before the removal from the fire, eight tablespoonfuls of cream were poured in and a moderate quantity of loaf-sugar added." The proportions of milk, cream, and arrowroot were made to depend upon the age and digestive

powers of the infant. For a healthy infant of a month he gave from three to four ounces of milk, one-half to one ounce of cream and a teaspoonful of arrowroot, to one-half pint of water. For older children the quantity of milk and cream was gradually increased to one-half or two-thirds milk and from one to two ounces of cream; the gelatin and arrowroot remaining the same.

Judson and Gittings state that in the seventies Meigs advised a mixture of equal parts of milk, cream, lime water, and arrowroot water, sweetened with a little sugar. This formula, which they mark as "the fountain-head" of all the later advances in milk modification, is not mentioned in any of the several editions of his work, and must have been obtained from some other source. It would really seem more fitting to mark the earliest formula of Meigs as "the fountain-head," since it was success in the use of this formula that led to the preparation of a monograph entitled *Food for Babies*, by William Henry Cumming, M.D., of Williamstown, Mass., and published in New York in 1859. In the preface to his work he eulogizes the writings of the elder Meigs, and points out that it was the success he met with in the use of the Meigs formula that stimulated him to a careful study of the subject of infant feeding, the result of which he so well presents in the work under discussion. This author approaches more nearly to a scientific modification of cow's milk than anyone who wrote prior to his time or for many years after. He says: "The milk that is adapted to a newborn calf is not suitable to an infant. It must be modified, or else it will do harm rather than good. Everyone knows that an infant cannot bear pure cow's milk, and everyone adds more or less water to weaken it. There is too much casein in cow's milk, and the infant cannot digest it. There is almost three times as much as in human milk, as seen by the following tables:

"In 1000 parts of cow's milk there are of	Butter	38.59 parts.
	Casein	40.75 "
	Sugar	53.97 "
	Water	866.69 "
"In 1000 parts of human milk there are of	Butter	20.76 parts.
	Casein	14.34 "
	Sugar	75.02 "
	Water	889.88 "

"Therefore, to reduce the casein of cow's milk to the proportion found in human milk, we must add one and four-fifth times, or nearly twice, as much water. Milk thus diluted will not be likely to disagree with the child's digestion; but after a time one will find that the child is not thriving on this diet, for the reason that the proportion of butter has been diminished with that of the casein from 38.59 to 13.58—just about two-thirds of the proportion existing in human milk (20.76)—a proportion which is far less than the infant demands.

"To those at all familiar with the elements of arithmetic it will be evident from comparing the relative proportions of the ingredients that dilution of ordinary cow's milk will never enable us to imitate the composition of human milk. It is possible, however, to obtain a milk having this composition in two ways: First, by taking the upper third of cow's milk that has stood for four or five hours, which has the following composition: butter, 54; casein, 38; sugar, 52; water, 856. By adding to this sugar 142, and water 1458, and dividing by 2.6 to reduce it to thousandths, we obtain a mixture having practically the composition of human milk. Another and in warm weather a better way is by taking milk from the latter half of that given by the cow. The first part contains very little butter, the last part is very rich—about 56 parts in 1000 in butter. This milk when diluted with one and one-half parts of water and properly sweetened resembles ordinary human milk."

That he appreciated the necessity of varying dilutions for varying ages is evident from what follows: "Mother's milk for the first two weeks after birth has a peculiar composition. From its first appearance it gradually changes until it becomes ordinary milk. Our mode of feeding involves the imitation of these several qualities of the milk. We call our substitute 'artificial human milk.'" The method of obtaining a milk to meet these various requirements is indicated in the following table, which shows the quantities of milk, sugar of milk, and water required for the various age periods. His formulæ are expressed in the proportions of the different ingredients contained in 1000 parts of milk. Thus 1000 parts of the milk taken from the upper third of cow's milk which has stood for four or five hours, as previously stated, contains 54 parts of fat, 38 of proteids, 52 of sugar, and 856 of water.

In order to obtain the proper proportions of the ingredients for the different age periods, he adds to this top milk, which is especially rich in fats, certain amounts of water and milk sugar. Being curious to know exactly what this table represented I have worked it out, and in so doing obtained some very interesting results.

He prescribed a mixture of the following strength:

	F.	P.	S.
For the age of 1 month	1.5	1.1	7.4
" " 2 months	1.8	1.3	7.4
" " 3 "	2.0	1.4	7.4
" " 4 "	2.3	1.6	7.4
" " 5 "	2.6	1.8	7.4
" " 6 "	2.7	1.9	7.4
" " 7 " and 8 months	2.9	2.0	7.4
" " 9 " to 10 "	3.0	2.1	7.4
" " 11 " to 13 "	3.1	2.2	7.4
" " 14 " to 17 "	3.3	2.4	7.4
" " 18 "	3.5	2.4	7.4

For children under one month he made his mixtures by diluting the upper eighth of a bottle which had stood for four or five hours, making his dilutions much greater.

It is to be assumed, since Cumming does not state that the analyses which he used are borrowed from others, and since they do not quite agree with any of those made prior to his time, that he made his own. In so doing he has been in error in considering the top milk he used—the upper third of milk which has stood for four or five hours—to contain but 5 per cent. of fat. According to Chapin's table, this milk should contain about 10 per cent. of fat, which would, of course, practically double the fat percentages indicated in his table. Had he restricted himself in the preparation of his mixtures to the milk obtained in the latter half of the milking, assuming as he does that this was a 5 per cent. milk, he would probably have more nearly obtained the results he thought he had obtained by the other method.

Cumming fully recognized the limitations of these formulæ. Thus he says "this schedule is arranged to suit the wants of vigorous children, but in using it great care and skill are needed. Regard must be had not to the mere age, but to the condition of the child. One child goes on prosperously to the age of six months; he is in every sense six months old. The dilution directed for that age will suit him exactly. Another during his third or fourth month is sick and feeble. On learning these facts and observing his condition we should say: this child was born, it is true, six months ago, but his time has been ill spent; he has not made the usual progress; we must reckon him as only four or five months old. To such an one we give the milk suited to the seeming age. It is indeed always safer to begin with milk somewhat more diluted than the child's age indicates and to increase its strength as the case will permit. It is less hurtful that the food should be insufficient than that it should be indigestible. . . . If a child using this milk becomes sick it is well to diminish at once the strength of his food to that of a child three or four or sometimes (in severe cases) six months younger."

He also appreciated the value of increasing the percentage of fat where there existed a tendency to constipation; thus he says: "It will sometimes happen that, while using milk prepared according to the foregoing directions, constipation may occur. An addition of butter to the milk will here be useful." He follows this by an explanation of the manner in which the fat percentages may be increased.

He evidently met with the same obstacle in applying this plan of feeding that often confronts us in our attempts to feed infants from the laboratory, namely, the cost. He says "this prepared method of artificial lactation involves much care and expense. The excellence of our plan is not that it costs nothing, but that it will repay the parent

for all the labor and money expended. How much money is yearly expended in securing medical aid for children who need not medicine but food?"

These quotations from this very interesting work are sufficient to make it evident that a successful effort at definite percentage feeding was made at an earlier period than we have hitherto thought. It is difficult to determine how extensively this booklet has been read, but since one finds no reference to it in the text-books on pediatrics, it is probable that this careful, observing, and original author made a valuable contribution to the elucidation of an obscure subject without even obtaining an audience for his opinions.

The development of percentage feeding beyond this point, including the works of the younger Meigs, of Rotch, and others, is so familiar to all of us that it is unnecessary to consider it in this communication.

It is sufficient to say of the *starchy* and *mucilaginous preparations* and the various *animal broths* and *teas*, that they have been prominent constituents of the infant's dietary in the period covered by the literature which has been reviewed and probably for many years prior to that time. Many of the older writers preferred them to milk in any form, while the majority of those who preferred milk permitted the use of these substances as additional foods. Still another class prepared their paps, panadas, etc., with milk instead of water, thus combining the two methods.

The so-called pap or panada—the terms are sometimes used synonymously and sometimes to describe different preparations—have been very variable in composition. Des Essartz (1760) gave the following directions for pap: "Put in a copper or iron kettle (preferably the latter) some fine wheat flour. Cover this with cold cow's milk added little by little. When thoroughly mixed cook until thick." The degree of thickness should vary with the age of the infant.

Armstrong (1783), on the other hand, used "the crumb of stale bread, roll, or biscuit boiled in soft water to a proper consistency sweetened to taste like new milk." This latter method probably conforms more nearly to that adopted by the generality of writers.

Broths have been almost universally sanctioned as a part of the diet of the latter months of the first year. Only one writer—Marshall Hall—seems to have placed them before all other food preparations.

Before bringing this essay to a close, it seems desirable to consider the implements which have been used in the administration of artificial foods. They are the boat, the spoon, the sucking horn or bottle, and the pot of Dr. Hugh Smith. But one reference is made to the last mentioned, and that is by Underwood (1789). "It is formed," he says, "in the shape of an Argyle or gravy pot, with a long spout rising from the bottom and pierced only with a few small holes at the end, which

is to be covered with a piece of vellum or parchment which, being left loose a little way over the spout, is as soft and pleasant to many infants as the breast. The boat, spoon, and horn are in no way comparable to it." He advised strict cleanliness in its use.

The spoon is referred to but not recommended by Des Essartz (1760). He graphically describes and bitterly denounces the filthy methods resorted to by nurses in the use of this instrument. He says: "After putting the pap in the spoon they carry it to their mouths, cool it off, return it to the spoon and then give it to the infant." "Some nurses, not wishing to use the spoon, place their index fingers in the food, which after cooling, they permit the infant to suck."

I have endeavored to fix upon the date of introduction of the nursing horn or nipple, but without success. Among the writers I have consulted, Rosen von Rosenstein (1776) was the first to recommend the sucking horn. From his reference to it, one would infer that it had not been much used outside of Russia prior to that time. He writes thus: "If we cannot procure a nurse and the mother cannot suckle her child, then we must accustom the infant to suck by means of a little instrument called a sucking bottle, which is universally used in eastern Bothnia with great advantage; but this machine ought always to be kept clean. It is to be made of a horn, the smaller end of which may be fastened to a tanned skin of a cow's teat, or if this is not to be procured we may use any other thin skin pierced with many small holes."

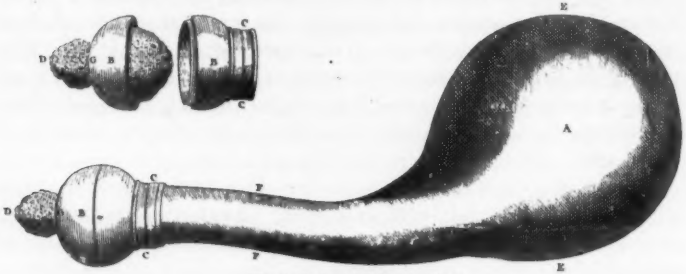
Armstrong (1783) describes this instrument in the following manner: "The horn made use of for suckling is a small polished cow's horn which will hold about a gill and a half; the small end is perforated and has a notch around it to which are fastened two small bits of parchment, shaped like the tip of a finger of a glove and sewed together in such a manner that the food poured into the horn can be sucked through between the stitches." This description marks a slight improvement in the manner of preparation of the horn and suggests a new substance for the artificial nipple.

In 1794 Moss described "a machine made of horn or *tin* so contrived that the child sucked his food from it as from a breast."

In 1786 Baldini described what was probably the first glass nursing bottle, a sketch of which is submitted for inspection. (See illustration.) He says of it: "This bottle, made of glass or crystal, is surmounted by a hollow metal knob which is gilded so that it will neither rust nor collect verdigris. This knob is divided in its centre into equal portions which screw together. The distal portion is perforated by a small aperture, through which a portion of a sponge placed in the hollow part protrudes. The protruding portion of the sponge represents the portion from which the child sucks."

For the poorer classes he advised "an ordinary bottle capped with

a piece of chamois." The chamois was "open at the end and surrounded a piece of sponge which extended into the neck of the bottle and protruded through the opening described. He advised that this apparatus "be washed many times each day in tepid water."



The first glass feeding bottle.

Chambon (1799) recommended a feeding bottle, evidently referring to a glass bottle, "the orifice of which was closed with a linen rag or piece of sponge to prevent the milk from running too rapidly." He says, "I will not describe the methods which have been published to simulate the breast nipple," from which one would infer that there had been many. He, like his predecessors, insists upon scrupulous cleanliness in the care of this instrument, "as otherwise it contracts a disagreeable taste, disgusts the children, occasions vomiting, and infects the milk, causing it to change rapidly in the stomach."

After this date both the horn and bottle were recommended, the horn rather more than the bottle, until Dewees, in 1825, recommended "a flat oblong nursing bottle covered with a properly prepared cow's teat." He insists that "much care be given to preserving it sweet. One should never put a second supply of milk or food upon the remains of a former. The bottle should be emptied after each nursing and immediately cleaned with hot water; it should then be thrown into and kept in a basin of cold water in which there is a little soda dissolved, and, before being used, well rinsed with clean cold water."

He prefers the heifer's teat to any other form of nipple, and urgently recommends that it be prepared "by those who understand this art." It must not be too large or permit too rapid a flow of the food. It should always have a piece of sponge in it to control the flow. Both the teat and the sponge should be well washed after each feeding and be kept in whiskey and water. Clean thread should be used each time the teat is tied on." He also refers to a tube which was in use at this time, and condemns it, owing to the difficulty of keeping it clean.

In 1833 Dendy recommended as a nipple "washed leather or the teat of a young heifer, in which a small piece of sponge is placed in

imitation of the pores of the nipple, to prevent too rapid a flow of milk. The first is more easily kept clean, but the latter more acceptable to the infant; indeed, more eligible, as it brings the necessity of constant cleaning." He advised keeping it between feedings in rose or distilled water to which a few drops of spirit of wine had been added.

Combe (1840) advised either washed leather, chamois, or a few folds of fine, soft linen, pierced with a small hole for the mouth of the bottle. "Sometimes a small piece of sponge covered with a rag, or the *artificial cork nipple recommended by Dr. Bull*, may be preferred. Whatever material is used, great care must be taken not to have the holes too large." This author quotes Erdman as saying that "the peasantry in Russia, even at this late date, are using, instead of a nursing bottle, a cow's horn with a small hole at the point, over which a cow's teat is tied. The teat is placed in the child's mouth, the milk poured in at the larger end of the horn and the child left to suck at pleasure." And Van Ammon says that "among these people the horn is not cleaned and frequently the teat passes into a state of putrefaction."

Churchill (1850) used chamois or cow's teat for a nipple, preferring the latter, and also described a thin elastic cork nipple invented by M. Dardo, of Paris, and *one of ivory* from which the earthy matter had been removed and which was flexible and elastic. He did not consider them as satisfactory as the calf's teat, "being far too short."

The first reference I have been able to find to a rubber nipple appears in the work of Tanner, published in Philadelphia (1861). He advises a nipple formed of *vulcanized India rubber*. S. Barker (London, 1864) recommended a nipple made of ivory, cork, *India rubber* or wash leather.

The high mortality in earlier times among the artificially fed (six in eight, according to Dr. Merriman, quoted by Dendy), in the light of what has gone before, would seem to have been not so much dependent upon defective formulæ as upon the poor methods of administration and probable lack of care in collecting and preserving the milk.

NOTE.—Since writing the above I have discovered that the first communication of William Henry Cumming, M.D., on the subject of diet in early life appeared in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for July, 1858, N. S., vol. xxxvi., p. 25, under the title, "On Natural and Artificial Lactation." This article formed the basis of his monograph. It demonstrates clearly that the chemical analyses quoted from the monograph were the results of his own work.

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A CASE OF GANGRENE OF THE LUNG CURED BY OPERATION.*

By David Riesman, M.D., A. C. Wood, M.D.,

and

G. E. Pfahler, M.D.,

of Philadelphia.

The history of the case is as follows:

I. P., a negro, aged sixty-three years, born in Delaware, was admitted to my wards in the Philadelphia Hospital on July 22, 1902. His mental condition was such that a complete history was not obtainable, but it was ascertained that his family history was good and that his own health had always been satisfactory.

* Read before the College of Physicians of Philadelphia, December 3, 1902.

The illness, on account of which he entered the hospital, began four days prior to admission, with chill, pain in the right side, and cough. Examination showed the patient to be an emaciated man, with excessively tortuous temporal arteries, and hard, beaded radials, with arcus senilis and contracted pupils. His skin was hot and dry, the tongue coated, the breath offensive, the temperature 103.6°, the pulse 110, hard and incompressible, the respirations 36. The chest showed diminished expansion on the right side. The percussion resonance was impaired over the middle of the right lung posteriorly, and in the middle of the right axillary region. Over this dull area fremitus was increased. Auscultation did not afford any satisfactory revelations. The heart sounds were feeble, except for the second aortic, which was accentuated.

The temperature remained elevated—between 102° and 103.4°—for two days. During the night of July 24th it fell rapidly from 103° to 98°, without any sweat. The respirations dropped to 28, the pulse to 88. Within a few hours, however—by 11 A.M.—the temperature had again risen to 101.6°, declining by the following morning at eight to 97.8°.

Examination at this time revealed very little of moment in the chest. No distinct area of consolidation could be discovered, and, judged by the physical signs, the man's condition had greatly improved. The symptoms, however, did not show a corresponding amelioration. Despite the fall in temperature, pulse, and respiration rate, the patient's state appeared grave. He was delirious and struggled to leave the bed, had insomnia, coughed a great deal, and passed urine and feces involuntarily. During the time in which the quantity of urine was measurable, it was from twenty-two to thirty ounces; it contained albumin and an abundance of hyaline and granular casts, was acid in reaction, and had a specific gravity of 1020. The bowels were loose, greenish in color, and very offensive. There was no enlargement of the liver or spleen.

The temperature remained decidedly subnormal for four days, between 96° and 98°, the highest point in the day being reached at either 8 P.M. or 2 A.M. Only once during the four days did it ascend above 99°. The breath was offensive, especially during coughing, and on July 28th the resident physician, Dr. Dalby, noticed that the sputum had a gangrenous odor. In a specimen examined at this time I was not able to find elastic tissue or fatty acid crystals. Tubercle bacilli were also absent.

An examination of the chest made on July 28th showed the following: Slight impairment of resonance on the left side, in the first and second interspaces in front; a normal note elsewhere over the left chest. On auscultation the breath sounds were found to be feeble over the entire left side, including the area of slight dulness. Here, however, the expiration was a trifle prolonged, but neither harsh nor bronchial. On the right side nothing was found in front; posteriorly, however, important physical signs were discovered. There was a dull patch to the inner side of the lower half of the scapula, in the scapulovertebral space, the dulness extending downward and forward to just behind the postaxillary line. Over the dull area, especially in the spinal gutter, tactile and vocal fremitus were increased. On auscultation bronchial breathing could be heard over a small area inside of the

lower half of the scapula, close to the spine, at the level of the fifth rib. Below the angle of the scapula the breath sounds were normal,

Fig. 1. Before operation.

but became faint in the axillary region. The pulse was feeble and almost thready; the breath gangrenous. The patient was delirious and had to be restrained. Dr. Wood saw him with me at this time,

and agreed as to the advisability of operation. The man was transferred to the surgical wards, and, at my request, Dr. Pfahler made an

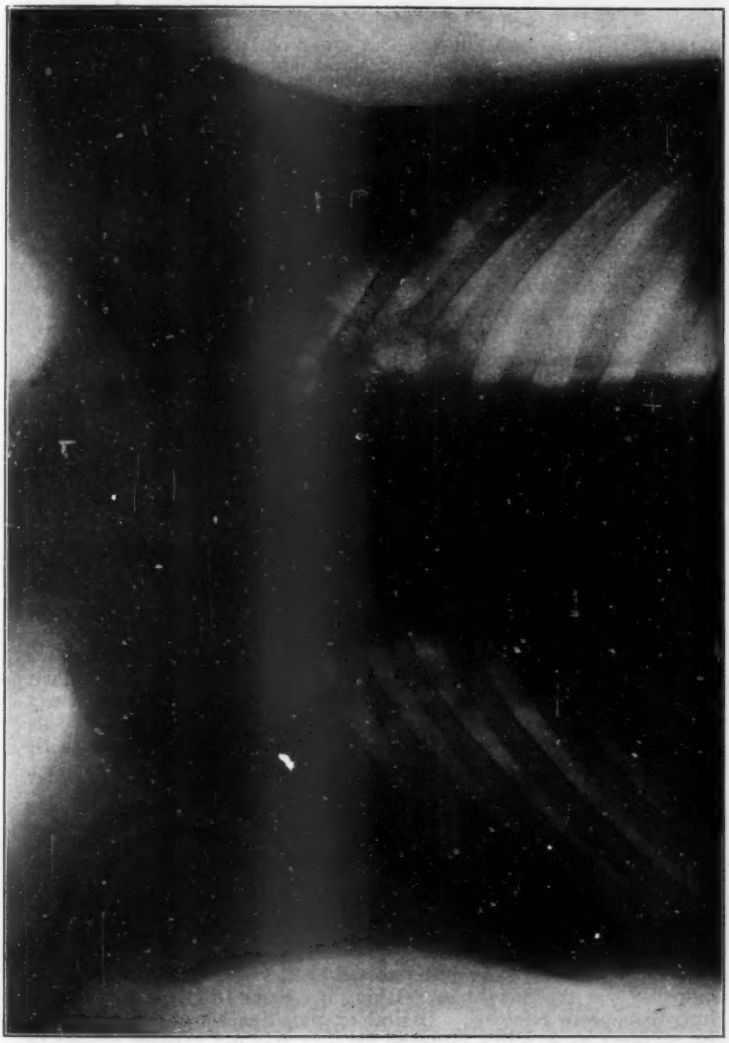


FIG. 2.

Before operation.

Several months after operation.

X-ray examination. Inspection with the fluoroscope showed impaired movement of the right half of the diaphragm, with a distinct shadow at the right apex. The lower portion of this shadow was on a level

with the base of the spine of the scapula. A negative was made, which was developed while the patient was being etherized and prepared for operation. This negative exhibited more distinctly the area involved, and showed a dense wall surrounding a lighter area in the upper part of the right lung. The lower portion of this wall was on a level with the base of the spine of the scapula, and apparently included all the lung space above this point. The patient moved during the exposure, and thus spoiled what would otherwise have been a good negative. Physical examination just prior to the administration of the anæsthetic showed, as before, a small patch of dulness and bronchial breathing in the area between the spine and the right scapula.

Guided by the physical signs and by the information furnished by the radioscopic examination, we were able to determine in advance where to make the incision and which rib to excise, the fifth being the one chosen.

The following are Dr. Wood's notes upon the case:

"I saw the patient referred to in the foregoing report through the courtesy of Dr. Riesman on July 28th last. The most striking feature was the very offensive odor that was observed upon entering the room, which became more pronounced as the patient was approached. The odor that came from the man's breath was typical of gangrene. The other features that impressed me were the normal temperature and the confused mental condition of the patient. The result of the physical examination is fully detailed above. I had no hesitation in coinciding with Dr. Riesman in the diagnosis of gangrene of the lung, and in the opinion that an early operation should be performed. The only point that seemed in doubt was whether the patient would survive the operation, but, as we felt that recovery was impossible by any other means, we considered it proper to give him this chance.

"The gangrenous area of the lung had been very carefully outlined by Dr. Riesman and Dr. Pfahler, and the latter had taken an excellent skiagram, which fully confirmed the location of the lesion as previously determined by physical examination.

"The operation was performed July 29th. Just before the anæsthetic was administered, Dr. Riesman again, at my request, outlined the area of dulness, which was on the level of the fifth rib, on the right side posteriorly, between the inner border of the scapula and the spine.

"Chloroform was administered until anæsthesia was complete, when ether was substituted. The skin was then cleansed in the usual manner, and the fifth rib exposed by a slightly curved incision, an inch and a half or two inches of it being resected by the subperiosteal method. The visceral and parietal layers of the pleura were found to be adherent, and dark and lustreless in appearance. The gangrenous portion of the lung was found to be just beneath the pleura, so that no delay or difficulty was experienced in reaching it. Some fragments of necrotic lung-tissue were removed. Digital examination showed the cavity to be as large as a man's clenched fist. It was not thought proper to irrigate the cavity, but the walls were gently cleansed with the aid of gauze sponges, which brought away all loose dead matter. The cavity was then packed with sterile gauze, and the usual dressings were applied.

"The patient bore the operation very well, and did not seem any worse in consequence. The wound was redressed daily, the packing and any sloughs that appeared being removed, after which fresh packing was introduced. The discharge was very profuse at first. The breath rapidly lost its foul odor, and, although the wound remained very offensive for some time, it gradually lost this character. The delirium persisted for some days, but became less and less pronounced, and finally disappeared entirely.

"Instead of a subnormal temperature, which was present before operation, the temperature rose immediately, reaching 101°. The pulse was 112 on the evening of the operation. On the fourth day the temperature reached 102.6°, pulse 104. From this time both temperature and pulse gradually declined. Cough continued to be a prominent symptom, but became less troublesome. The general condition of the patient changed for the better in a very satisfactory manner.

"While dressing the wound it was noted that air was expelled violently when the patient coughed, showing that a rather large bronchus opened into the cavity. The volume of air thus escaping from the wound diminished continuously as the cavity healed."

On August 24th a note says: "Patient still has cough, but otherwise is in a fair condition. Air still comes through the wound, but the probe shows that the cavity is decreasing in size. The patient feels well and wants to sit up."

From this time on the convalescence was rapid and satisfactory.

Some of the points of interest brought up by this case are, first, the use of the X-ray as an aid in locating the pulmonary lesion. While the procedure is no longer new, another instance of its value is worth recording. Although the skiagraph confirmed the physical signs accurately and in no way modified the treatment, it was very satisfactory to have this confirmatory evidence. It must be admitted that physical signs are sometimes misleading, and it is in these cases that the X-ray gives invaluable service. Tuffier (*Revue de Chirurgie*, August, 1901) advises that, when skiagraphic findings do not coincide with the results of auscultation and percussion, the latter be ignored and the operation be done according to the evidence furnished by the former. He cites a case in which the skiagraph showed a lesion toward the base of the lung, while the stethoscope indicated a higher site. The incision was made at the point indicated by the stethoscope with negative results. The next rib below was then resected, and the focus was discovered in the place shown by the X-ray. The same author reports eight cases in which he has applied radiography to pulmonary affections. The results were extremely satisfactory in five instances and negative in three. In some pathological conditions the X-ray fails entirely, but gangrene of the lung has been found to cast distinct shadows. In accepting the X-ray evidence, it is necessary to be assured of the fact that the plate is satisfactorily clear. If doubt exists it is better to discard it altogether. In order to be as certain as

may be, it is desirable always to have two skiagraphs taken, and to note whether they conform with each other.

The importance of definitely locating a lesion of the lung before undertaking any operative procedure will appeal to everyone. On this point Tuffier states that operations on the lungs when the lesion was accurately diagnosed beforehand were successful in 71 per cent. of the cases—that is, that the mortality was 29 per cent., while the mortality was 60 per cent. in the cases in which there was a mistake in the diagnosis. Of 300 cases collected by this author, the lesion was incorrectly diagnosed in 48.

The resection of a rib may be done under local anæsthesia if the condition of the patient will not warrant the use of a general anæsthetic; but in our case the delirious condition of the man made him an unsuitable subject for the former. When a general anæsthetic is necessary, chloroform is usually to be preferred.

The resection of ribs and the pleural opening should be ample in cases of pulmonary gangrene. This is more essential in these cases than in abscess of the lung, as the healing process is slower and it is necessary to keep the external opening patulous until the cavity is entirely closed. With a liberal opening, also, the wound may be drained with gauze, which I believe to be more efficient and suitable in these cases than tubes.

When the parietal and visceral layers of the pleura are adherent the lung may be opened immediately, but all operators agree concerning the desirability of securing this condition before attacking the lesion. When adhesions do not exist, therefore, the two layers should be stitched together around the proposed opening into the lung, which may be made at the end of forty-eight hours or sooner, if the patient's condition demands earlier relief.

Some operators advise against irrigating the cavity in these cases, and with these I am in entire accord; others are equally convinced of the value of this procedure. Those that hold the latter view should follow the method advised by Cotterill: "The fluid should be a mild antiseptic (not carbolic lotion); it should be warmed to about blood heat; it should be injected slowly and without force, great care being taken that it runs out as fast as it runs in. The patient should be rolled over into such a position that it is impossible for a large volume of the lotion to collect in the chest at one time, and, by its weight, embarrass the heart. . . . . The fluids I prefer to wash out with are: boric lotion, a solution of creolin, or a solution of izal, the latter of which is a particularly useful deodorizer."

Herezel states that about one-fourth of all the recorded operations upon the lungs have been for gangrene. Of 91 cases of pneumonotomy for gangrene, 60, or 61 per cent., were successful. Garré reports 122

cases operated upon for pulmonary gangrene, of which 66 per cent. were cured. He states that but 20 or 25 per cent. recover without operation.

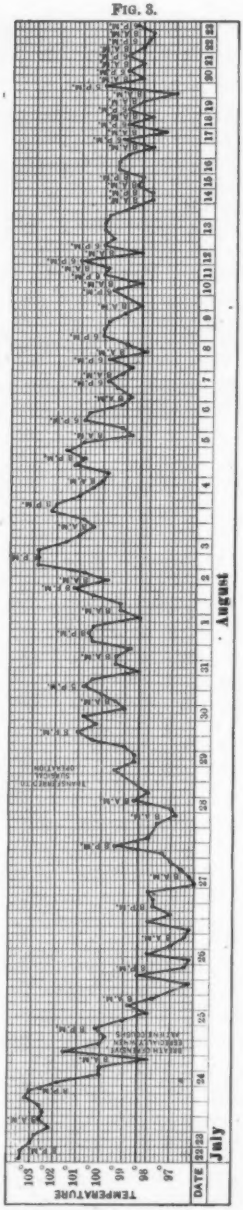
The patient's present condition is most satisfactory. He feels strong, his mind is clear, and he has become a useful helper about the ward. Physical examination shows a slight depression below the right clavicle. The percussion-note is the same on the two sides in front, but it is slightly impaired in the right axilla and below the operative wound for a distance of one and one-half inches. Auscultation shows increase in vocal fremitus, and harsh breathing in the neighborhood of the wound—not extending more than an inch above this. The urine has a specific gravity of 1018, and contains a faint trace of albumin, but no casts. The man has gained between thirty-five and forty pounds in weight. There is a slight discharge from the sinus, but the indications are that it will soon be closed.

While the chief interest of this case centres in the happy results of the operation performed by Dr. Wood, there are several points of importance to which brief allusion will not be out of place. The first of these is the cause of the gangrene. The history of an acute onset during fair health, with chill, cough, and pain in the side, suggests that the primary condition was lobar pneumonia. The question why this so rapidly—apparently within less than ten days from the time of onset—passed into gangrene cannot be answered except in a speculative way. It must be remembered that the patient had pronounced arteriosclerosis and albuminuria, and it is admitted by all that such conditions favor the development of gangrenous processes in the lung.

Lobar pneumonia is an accepted precursor of gangrene; but Aufrecht,[1] among 1501 cases of pneumonia, did not find a single case of gangrene—a most remarkable circumstance. He also cites Grisolle, who, in a collection of 305 cases of pneumonia, found none followed by gangrene, while among 70 cases of pulmonary gangrene there were only 5 in which the condition supervened upon pneumonia. Osler,[2] however, observed gangrene three times in 100 cases of pneumonia (3 per cent.); and in Norris'[3] collection of 500 cases from the Pennsylvania Hospital, there were three instances of gangrene—a proportion of 0.6 per cent. Tuffier,[4] in his collection of 74 cases, found pneumonia to be the etiological factor in more than 30, while Pomeranzew[5] found 5 cases of gangrene among 727 cases of pneumonia.

In the only other case of gangrene that has come under my own observation—one that I did not see during life, but upon which I made the autopsy—the condition also followed lobar pneumonia. Other causes of gangrene that need merely be mentioned are embolism, the aspiration of foreign bodies and of putrid material from the upper air-passages, wounds of the lung, tuberculosis, and the rupture of an empyema into the lung. Embolic gangrene has been observed after

FIG. 3.



abdominal operations in puerperal sepsis, as a sequel to middle-ear disease, and secondarily to other abscesses and pyæmic foci. The fetid material that is the cause of aspiration-gangrene may come from the pharynx, from the œsophagus in cases of obstruction or rupture, or, as in a case reported by Packard and Le Conte,[6] from a bronchiectatic cavity. Gangrene also occurs as a rare effect of compression by aneurisms or tumors. Diabetes, typhoid fever, alcoholism, and—according to Gee and Herringham[7]—scurvy, are predisposing causes of gangrene. It is probable that in the majority of cases of gangrene, the system at large or the lung itself was previously in a state of lowered vitality.

The second point that I desire to emphasize is the absence of fever in our case. Fever, according to the majority of writers, is an important symptom of gangrene. Aufrecht[8] states that he has never seen it absent. Usually it is high—40° C. (104° F.) and over. At times it is remittent. As the temperature chart shows, the gangrene in our case pursued its course, not only without fever, but with a subnormal—almost a collapse—temperature. Pulse and respiration were equally unsuggestive of serious trouble, and it was only the man's general condition, his delirium and prostration, that made us realize that he was in grave danger. At the Philadelphia Hospital the opportunities for observing anomalous types of acute pulmonary disease are abundant. Only recently I saw a case of complete pneumonic consolidation of the left lung, typical at autopsy, and complicated with purulent pericarditis, in which there had been no fever.

The third point worthy of mention is the character of the sputum. As stated in the notes of the case, there was no elastic tissue, and fatty acid crystals were likewise absent. The odor, however, was characteristic of gangrene. In the diagnosis of pulmonary gan-

grene the sputum deserves careful attention. In typical cases it separates into three layers, the lowest consisting of globular masses with a tendency to confluence, the highest being frothy and having masses of dirty sputum depending from the surface. The intermediate stratum is composed of a greater or less quantity of turbid, opaque fluid. When a part of the bottom layer is boiled with a 2 per cent. solution of potassium hydrate and examined microscopically on a slide, wavy bundles of elastic tissue are commonly found; but elastic tissue may be entirely absent. This fact is explicable on two grounds: first, the gangrenous process may have been arrested, the cavity no longer spreading, and, secondly, the elastic tissue may have been dissolved by the peptonizing action of the fluid—a result that is probably due to bacterial activity. It has been shown by Müller and by Simon,[9] to quote an analogous phenomenon, that the pneumonic exudate is dissolved by a proteolytic ferment. The fatty acid crystals are frequently absent. They are usually found in old cases of gangrene; ours was, of course, acute. In some cases of gangrene the sputum presents nothing peculiar, and the destructive process in the lung is discovered only at autopsy.

An attempt has been made to differentiate the odor of fetid bronchitis from that of gangrene. Aufrecht compares the former to the smell of stale cheese, and the latter to that of the fluid of manure.

It is scarcely necessary to discuss the other diagnostic features of gangrene. The sputum and the fetor of the breath are, as Osler[10] says, the distinctive features. The important point is accurately to locate the involved area. When the gangrenous process is circumscribed physical examination usually renders this possible; it serves at least to focus attention upon a particular spot in the lung. When, however, the process is more or less diffuse or the foci are multiple, accurate delimitation is difficult. In the circumscribed form there may be the signs of a cavity or those of consolidation. When the symptoms are clear and physical examination gives but dubious results, a careful search should be made for the presence of râles, as their detection may be the only clue to the situation of the trouble. Errors are, however, frequent. Strange to say, the physical signs are likely to locate the focus either too high or too low; the latter is more often the case. Furthermore, they do not give an exact idea as to the depth of the gangrenous area beneath the surface of the lung, and they often fail to map out its actual size. Usually the gangrenous cavity is found to be much larger than was expected. Gangrene has occasionally been mistaken for empyema, as in a case reported by Körte.[11]

Exploratory puncture naturally suggests itself as an aid in diagnosis and localization, but, on account of the danger of causing infection of the pleura with consequent empyema, or by carrying the needle that

has been infected by its penetration of the cavity into a healthy part of the lung, of producing a spread of the infection throughout the lung, exploratory puncture is better avoided. It is condemned by Lenhartz,[12] by Tuffier,[13] and also by Terrier and Reymond ;[14] the last-named authors think it permissible only as a prelude to operation.

Schulz[15] states that it ought not to be used while the thorax is unopened, but considers it one of the most valuable methods for locating the diseased focus after the thorax has been opened.

As has been pointed out by Dr. Wood, the X-ray is of great value in the diagnosis, as it usually indicates with fair precision the size and position of the gangrenous focus. Depending upon whether the cavity is full or empty, there will be either a dark shadow or a light area in the affected region of the lung. In addition, fluoroscopic examination will show a lessened mobility of the diaphragm on the diseased side. I would suggest that in hospitals in which radiographic examinations can be made with facility, every case of acute lung trouble in which abscess or gangrene is a possibility be subjected to such an examination.

Prognosis. In acute forms of gangrene the prognosis is better than in those that are chronic. Metapneumonic gangrene has a decidedly larger percentage of recoveries than has gangrene due to embolism, aspiration, or bronchiectasis. In Tuffier's table of 71 cases, showing the relation of etiology to results after operation, there were 55 cases of gangrene following inflammatory affections of the lung, with 39 recoveries; 4 cases of bronchiectatic gangrene, with 1 recovery; 2 due to foreign bodies, with 1 recovery; 7 of the embolic variety, with 2 recoveries; 1 due to chest wound, with recovery; and 2 following perforation of the œsophagus, both ending fatally.

The mortality from gangrene without operation is necessarily very high—between 70 and 80 per cent. (80 per cent., according to Verneuill[16]). Under operative treatment the death-rate falls to 34 per cent., according to Garré and Sultan,[17] who have collected 122 cases, with 80 recoveries and 42 deaths. In Eisendraht's[18] series of 28 cases of pneumotomy for pulmonary gangrene, there were 20 recoveries and 6 deaths, with improvement in 2. One interesting feature alluded to by several writers is the apparently complete restoration of the diseased lung. In some cases reported by Lenhartz[19]—who has operated upon 25 patients for gangrene, 13 of whom recovered—physical examination and examination with the X-ray showed a perfectly normal lung where there had previously been a large gangrenous cavity. The author gives it as his opinion that there must be a re-formation of lung tissue. The second radiograph of our case also shows a restored lung. Whether there is a true hyperplasia of air vesicles or merely an enlargement of existing ones, it is not possible to say without other, especially experimental, data.

All writers upon the operative treatment of gangrene refer to the importance of adhesions. Their presence greatly increases the chances of a good result; their absence predisposes to pneumothorax and to the entrance of septic material into the pleura, with resulting empyema. Lenhartz advises that if the condition of the patient does not demand immediate pneumotomy, this operation should be performed in two steps, the lung being fixed to the chest wall at one time, and opened later. When, however, all the signs indicate that procrastination would be dangerous, it is best to open the lung without delay, care being taken to draw the organ into the wound and to stitch it, so as to guard against the occurrence of pneumothorax and empyema.

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ZOMOTHERAPY IN TUBERCULOSIS.

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SOME months ago two French scientists, Richet and Hericourt,[1] announced most favorable results in the treatment of tuberculosis with raw meat or its juice. They began two years ago to publish their observations, and during the last year both have written glowing accounts of the efficiency of this treatment. They have long been experimenting upon dogs, endeavoring to find some curative agent for tuberculosis; but all to no avail until they began to feed their dogs exclusively upon raw meat. Their dogs, 129 in number, may be divided into three groups. The first, composed of 30, received no treatment; the second, numbering

58, was treated by different methods, while the third, 41 in number, was fed on raw meat. At first the amount was unlimited, but later they found that 10 to 12 grammes per kilogramme of body weight of the animal was sufficient. The first and second groups lived, on an average, 52 days, while the dogs fed on raw meat lived, on an average, 227 days; in other words, the period of life was very nearly five times longer in the dogs fed with raw meat. From their experiments they conclude that cooked meat in any quantity is inefficacious, that meat deprived of its serum is moderately efficacious, and that muscle serum is as efficacious as raw meat. Raw meat they found also to act prophylactically.

The explanation of the action of the raw meat, although discussed at the Paris Conference in 1900, is still unsettled. Richet at that time attributed the beneficial effects to some body in the meat-juice that prevented the development of tuberculous granulations. According to Maragliano, meat acts as a stimulant, and therefore promotes the formation of an antitoxin in the body. More recently Richet has advanced a "metatrophic antitoxic action." The tuberculized animal, he says, dies by a slow and progressive intoxication of the nervous system. The active elements of the muscle serum preserves the nerve cell from a tuberculous intoxication.

Richet and Roux[3] have obtained favorable results in experimental meningeal tuberculosis in dogs. Twenty dogs were inoculated with tubercle bacilli in the spinal canal between the atlas vertebra and the occiput. Eleven of these were fed on raw meat and three survived, two of which were injected with tuberculin and did not succumb, as did one of the dogs which survived after being fed on cooked meat. Nine dogs were fed on cooked meat, and all died.

Chantemesse,[3] who first looked upon raw meat as a stomachic, has later taken an opposite view on account of his own observations. He injected two dogs with tubercle bacilli. One he fed upon raw meat; the other with cooked meat. The first remained sound and well; the second died.

Salmon[4] divided a number of dogs into three groups. The first, which received raw meat and was then injected, died as quickly as the controls. A second group, injected and then fed on raw meat, gained in weight and lived a fairly long time. In the third group treatment with raw meat was not begun until the disease had advanced considerably, and there was much loss of strength. On these raw meat exerted no influence. This author also calls attention to the fact that a dog which has apparently recovered from tuberculous peritonitis may still show at autopsy numerous fresh nodules in the peritoneum and internal organs and an extending tuberculosis.

Fränkel and Sobernheim[5] have published their results obtained by zomotherapy in tuberculous dogs and rats. Nine dogs and four rats

were injected with carefully estimated quantities of an emulsion of tubercle bacilli. Four dogs and two rats, fed on a mixed diet, were used as controls, and the remainder fed on raw meat. The dogs all died in six weeks. These authors suggest that Richet and Hericourt's results may be due to the fact that a non-virulent tubercle bacillus was used in the injections.

The literature on zomotherapy in human tuberculosis is more extensive, but no more conclusive. Duhoureau[6] mentions the case of his son, who, from smaller doses than those given by Hericourt, derived much benefit. Hericourt advises 600 to 700 grammes of raw meat, or the juice of 1000 to 1500 grammes of raw meat, per diem. In a recent article Hericourt[7] has collected statistics in zomotherapy in human tuberculosis. Besides eleven cases treated by himself, he reports twelve cases treated by others. These cases may be tabulated as follows:

TABLE I.

Site of lesion.	Number of cases.	Healed.	Improved.
Lungs	16	15	1
Glands	2	1	1
Skin	1	1	
Spine	1	...	1
Knee	1	...	1
Peritoneum	1	1	
Meninges	1	1	

It is but natural that anyone acquainted with pulmonary tuberculosis should, if the cases have not been selected, regard these uniformly good results somewhat skeptically.

Hericourt quotes, in addition, several favorable reports. Dr. Petit-Clerc[8] mentions three cases in the second stage of pulmonary tuberculosis who recovered under treatment by raw meat and fresh air. Dr. Sarge[9] has seen a case of pulmonary tuberculosis in the third stage recover under zomotherapy. Garnault[10] reports two cases in the second and third stages of pulmonary tuberculosis who apparently recovered under raw meat and intratracheal injections of orthoform. Josias and Roux[11] have followed zomotherapy as treatment in six cases of pulmonary tuberculosis in children, three of whom were in the second stage and did very well, and three in the third stage, who did not do so well. Three cases of meningeal tuberculosis were treated without favorable results.

At present the prevalent opinion is that Richet's method is only a better means of offering nourishment and of enabling a larger quantity

of food to be given. The resistance of gouty persons toward tuberculosis is, Weber[12] thinks, probably due partly to the meaty food. He recognizes, however, that due proportions of vegetables and fruits are of great importance. In some cases a fair amount of butchers' meat will stimulate the appetite enormously for all kinds of food, and render digestion more vigorous. Meat albumin, in contradistinction to milk albumin, writes Ross,[13] quickly and readily manifests its better qualities in the early observable improvement in the sufferer, and the benefit so obtained is not so easily undone as in the case of casein albumin. The cause, he thinks, is due to the fact that the adult has more muscle, and so needs more muscle-juice, or the muscle-juice contains more iron. Possibly, he says, the meat-juice contains some antitoxic substance. Browning the meat, he thinks, has little effect upon the real properties of serum.

Myosin albumin returns a maximum of nutrient for a minimum of effort, peptonizes readily, and is promptly absorbed, throwing little or no stress and irritating overaction on the stomach. But Bernheim[14] warns us that the benefit of alimentation is not measured by the quantity of food ingested, but by the quantity digested. The raw-meat treatment of Richet and Hericourt is, in effect, really suralimentation, but suralimentation in such a form that the majority of patients can stand it. "When, under the pretext of recovering the albuminoids, one submits the tuberculous patient to an exclusive meat diet, when one declares the carbohydrates—vegetables, sugar, cereals, etc.—to be secondary, the patient is deprived of an element primordially essential to repair, is given only an insufficient diet of phosphates, has his hyperacidity increased, and in place of increasing the artificial arthritism, which would be of value, a state of affairs is favored which would increase the susceptibility to the bacillus."

On account of the great expense, but few patients can carry out the raw-meat treatment as suggested by Hericourt, who advises that the juice of six pounds of rare beef, free from fat, bone, and cartilage, be taken daily. However, smaller quantities can be used advantageously. Two patients who took the full amount for several months made good recoveries. In one of these the disease was advancing quite rapidly. Many patients have been given beef-juice extracted from meat slightly browned, and it seemed to exert a very beneficial but no specific action.

In reviewing the experimental work done on this subject one is struck, as Fränkel remarks, by its meagreness. Chantemesse, Salmon, and Fränkel are apparently the only observers to repeat Richet's work. Fränkel obtained opposite results, Salmon's results were inconclusive, while Chantemesse, from experiments upon two dogs, upholds Richet. For this reason at the suggestion of Dr. Trudeau, and largely under his guidance, the following experiments were carried out:

The five dogs mentioned in Table I. were each inoculated in the external popliteal vein on July 17, 1901, with 2.5 c.c. of a translucent emulsion of tubercle bacilli. The tubercle bacilli were obtained by Dr. Baldwin from the sputum of a rapidly-advancing case of pulmonary tuberculosis. Hesse's agar was used to isolate the bacilli from the sputum, and after one transplantation to sheep serum tubes of dogs' serum (Prince's, q. v. infra.) were inoculated and the cultures used when eight days old.

Two dogs, King and Queen, were chosen as controls. They were fed on a diet of cooked meat, milk, and scraps from the table, but no raw meat. The remaining dogs received nothing but fresh raw beef. The dogs at once began to show but little desire for raw meat, and but one gained weight. The controls appeared much brighter for some time. The wounds on the legs remained open in all the dogs except Jester and Prince, where subcutaneous abscesses were found.

Jester, an old pug, died sixteen days after inoculation. On autopsy a perforation was found in the first part of the duodenum. A specimen of tænia saginata was found at this point of the bowel and was held to be the cause of the perforation, which led to slight peritonitis and death, probably from shock. Tubercle bacilli were found in the spleen, which was moderately enlarged.

During the fourth week all the dogs began to show signs of disease. Twenty-four days after inoculation Page died. Autopsy revealed general miliary tuberculosis of the lungs, general lymphatic glandular enlargement. Tubercle bacilli were found in the lungs and spleen. King, one of the controls, suddenly became very ill and died on the thirty-second day of the experiment. Miliary tubercles were found scattered throughout the lungs, and at the apices they showed beginning necrosis in the centre. A few hemorrhagic infarcts were found along the anterior borders of both lungs, and one spot of consolidation, size of a filbert, was discovered on posterior of left lower lobe. The spleen was very large and almost diffluent, and a general glandular enlargement was present. Lung, liver, and spleen showed many tubercle bacilli, while a few were found in kidneys, glands, and a cheesy focus in small intestine. The autopsy of Prince, who died on the thirty-fourth day, showed same condition in lungs and spleen, where a few scattered tubercles were seen. Enlarged glands, liver, spleen, and kidneys showed tubercle bacilli. The second control and last dog to die was Queen. The disease in the lungs had advanced further and conglomerate tubercles were found. Both lower lobes were nearly airless. The spleen was not so large as in the preceding dogs, but many miliary, grayish nodules were seen on section. Enlargement of glands was present. Tubercle bacilli were found in all the organs except the heart muscle. The heart's blood contained a few tubercle bacilli, but vast numbers were found in the liver, whose substance presented, on section, a peculiar translucent appearance, with a number of brown points surrounded by a narrow, yellow zone.

From this it is seen that the lungs and spleen bear the brunt of the infection, and that there was no greater difference between the pathological findings in the control and tested animals than among the tested animals.

The average life in the controls was thirty-four and one-half days; in the dogs fed on raw meat, it was thirty-one and one-half days.

TABLE II.

No.	Breed of dog.	Weight in kgr.	Quantity injected.		Injected July 17, 1901.	Food.	Death.	Days after injection.	Autopsy.
			Total c.c.	Per kgr. c.c.					
1 King.	¾ Spaniel.	11	2.5	0.22	Intravenously.	Mixed diet.	Aug. 18, 1901	32	Miliary tuberculosis of lungs; acute spleen tumor; tubercle bacilli from organs.
2 Queen.	Part Collie.	11.8	2.5	0.21	Intravenously.	Mixed diet.	Aug. 23, 1901	37	Miliary tuberculosis of lungs; tubercle bacilli from organs.
3 Page.	Mongrel.	9	2.5	0.27	Intravenously.	Raw beef.	Aug. 15, 1901	29	Miliary tuberculosis of lungs; tubercle bacilli from organs.
4 Prince.	Part hound.	17.3	2.5	0.14	Intravenously.	Raw beef.	Aug. 20, 1901	34	Miliary tuberculosis of lungs and spleen; tubercle bacilli from organs.
5 Jester.	Pug.	15.6	2.5	0.16	Intravenously.	Raw beef.	Aug. 2, 1901	16	Acute peritonitis; perforation duodenum; tænia saginata; tubercle bacilli from organs.

TABLE III.—WEIGHTS EXPRESSED IN PERCENTAGE OF NORMAL WEIGHTS.

Name.	July 17.	July 24.	July 31.	Aug. 7.	Aug. 15.	Aug. 22.	Aug. 29.
King	100	92.4	88	87	87	Dead	
Queen	100	105.6	102	98	92	82	Dead
Page	100	100.6	96	92	78	Dead	
Prince . . .	100	95.2	86.6	82	70	Dead	
Jester	100	96.2	86.4	Dead			
Average of controls	100	99	95	93	89.6	82	0
Average of tested	100	97.3	89.7	87	74	0	

Fearing that the tubercle bacilli used had been too virulent and that the dose given was too great, it was decided to repeat the experiment, using the attenuated tubercle bacilli grown by Dr. Trudeau for nine years under the name of R. 1. These tubercle bacilli are much attenuated, and injected subcutaneously in fairly large doses into guinea-pigs kill them only after many months. Accordingly on the 6th of December, 1901, six dogs were injected in the external saphenous vein with 2.5 c.c. of an emulsion of these attenuated bacilli. The dogs were divided into two groups. Four were fed on raw meat and given at the same time some fat and occasionally a little bread and dog biscuit. The two others were fed on a general diet exclusive of raw meat. The dogs, which had been fed well for some time previously, were all in good condition. Of the two chosen for controls, No. 5 was not in the condition of the other dogs, and shortly after the injection had a slight cough

which, however, soon cleared up. The dogs 1 to 4 inclusive gained weight for one week. Dogs 5 to 6 lost weight for a week, but then began to gain, and from that time on were in excellent condition and showed no loss of appetite. As seen from Table IV., dogs Nos. 3 and 4 died on the eighteenth and seventeenth days, respectively, after inoculation.

Their relative weights can be seen from the table. Dog No. 3 at first lost weight, but later gained considerable weight, and when he died, on May 4, 1902, 121 days after inoculation, weighed twenty-six pounds.

The last dog of the first group to die was No. 1, three-quarters Collie. This dog steadily gained weight for some months, but in July began to suffer from loss of appetite and refused to eat the raw meat. It was fed to him by hand for a time, and when he refused to eat it at all he was put on a general diet. Under this treatment he seemed to improve for a time, but later refused to eat anything but milk. He died finally on the 17th of August, 1902, 255 days after inoculation.

The two dogs used as controls after losing weight slightly at first began to gain. They never lost their appetite and were fed chiefly on "scraps from the table." Their weight never fell below normal, In August, 1902, both were subjected to the tuberculin test. Dog No. 5 reacted to 25 mgr. of Koch's tuberculin. Dog No. 6 received 25 and then 50 mgr. of Koch's tuberculin, but failed to react. This dog appeared well until about September 23, 1902, when he began to limp on his right fore foot. Two days later, after suffering for a part of one day from considerable dyspnœa, he died quite suddenly. The autopsy revealed a fibrous mass which had perforated (?) the aortic arch at the orifice of the innominate artery. A thrombus was found adherent to the aortic wall at this point.

On October 23, 1902, dog No. 5 died after showing slight signs of illness for several days. The left kidney was much enlarged, and the right kidney was the size of a small peanut and very sclerotic. The condition of the heart was similar to that found in dog No. 6, except that the acute endocarditis had more seriously damaged the aortic valve, which consisted largely of masses of vegetations. The mitral valve was slightly thickened, but not ulcerated.

From these figures it is seen that the test dogs lived on an average 110 days after inoculation and the two controls on an average of 308 days.

From the foregoing experiments on the treatment of experimental tuberculosis by raw meat, the following conclusions may be drawn.

1. That raw meat has no perceptible effect on the duration of experimental tuberculosis in dogs if the bacilli are virulent and a sufficient number injected intravenously.

2. That raw meat has no effect on the prolongation of the duration of experimental tuberculosis in dogs, even if the bacilli are attenuated, provided a reasonable quantity be injected intravenously.

3. That under the same conditions dogs fed on a mixed diet with no raw meat may live a much longer time.

Regarding the use of meat in pulmonary tuberculosis, it may be said:

1. That meat is highly essential in the dietetic treatment.

2. That much meat with a judicious admixture of carbohydrates, fats, etc., is essential to the treatment.

3. That rare meat is better than meat well cooked.

4. That meat-juice is of great value in suralimentation, as myosin albumin is easily digested by most patients—even the dyspeptic, and it affords a "maximum of nutrient for a minimum of effort." (In a few patients meat-juice causes diarrhœa and meteorism.)

5. That meat-juice can be taken when patients can take no other form of meat, *i. e.*, when there exists a marked repugnance to all solids.

6. That the juice from raw meat seems slightly, if at all, more beneficial than the juice from meat slightly browned.

7. That the disadvantages of preparing and preserving raw meat-juice more than offset its advantages. (Patients who object to juice from raw meat will willingly take that from meat browned.)

8. That meat-juice is of value, as it can be administered in the form of jellies, ices, etc.

TABLE IV.

No.	Breed of dog.	Weight in kgr.	Quantity injected.		Injected Dec. 6, 1901.	Food.	Death.	
			Total c.c.	Per kgr. c.c.			Date.	Days after injection.
I.	¾ Collie.	19.3	2.5	0.13	Intravenously.	Raw beef.	Aug. 17, 1902	255
II.	½ Spaniel.	13.09	2.5	0.19	Intravenously.	Raw beef.	Dec. 26, 1901	18
III.	Mongrel.	11.14	2.5	0.22	Intravenously.	Raw beef.	May 4, 1902	151
IV.	Fox terrier.	9.09	2.5	0.27	Intravenously.	Raw beef.	Dec. 25, 1902	17
V.	Bull and bound	19.1	2.5	0.13	Intravenously.	Mixed diet.	Oct. 23, 1902	323
VI.	Pug and Scotch.	10.8	2.5	0.23	Intravenously.	Mixed diet.	Sept. 24, 1902	294

TABLE V.—WEIGHTS EXPRESSED IN PERCENTAGE OF NORMAL WEIGHTS.

No.	Dec. 8, 1902	Dec 15, 1902	Dec. 24, 1902	Feb. 10, 1902	May 8, 1902	Sept. 20, 1902		Autopsy.
I.	100	102	109.8	115	116	Died Sept. 17, 1902	.....	Tuberculous abdominal glands, tuberculous nephritis and orchitis; endocarditis.
II.	100	103.9	100.2	Died	Dec. 26 1901	.....	.....	Tuberculosis of lungs, hæmatoma of stomach; pregnant.
III.	100	93	78.9	63	Died 106	May 4, 1902	.....	Tuberculous nephritis, tuberculous pulmonitis, hemorrhagic pericarditis (tub.?); endocarditis.
IV.	100	102.8	96.1	Died	Dec. 25, 1901	.....	.....	Pulmonary tuberculosis; pregnancy; tubercle bacilli in glands, spleen and liver.
V.	100	97	102.5	115	107	107	Died Oct. 23, 1902	Acute tuberculous endocarditis; adherent tumor containing tubercle bacilli ulcerating into aorta.
VI.	100	95	.....	.....	100.5	100.5	Died Sept. 25, 1902	Thrombus in aorta at orifice of innominate artery overlying erosion of aortic wall; adherent mass on outer wall of aorta; endocarditis (tuberculous?). On teasing no tubercle bacilli were found.

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NOTES FROM THE THROAT DEPARTMENT OF THE PATHOLOGICAL LABORATORY OF THE MANHATTAN EYE AND EAR HOSPITAL.[1]

(*a*) A RAPIDLY RECURRING BLEEDING POLYP OF THE SEPTUM NASI APPEARING TWICE IN A WOMAN, EACH TIME AT THE SEVENTH MONTH OF PREGNANCY.

(*b*) PAPILLARY ADENOMATOUS HYPERTROPHY OF THE MUCOUS MEMBRANE OF THE SEPTUM.

(*c*) A CYST IN THE LYMPHOID TISSUE OF THE PHARYNX.

(*d*) EFFUSION OF SERUM INTO THE NASAL MUCOSA IN CORYZA.

WITH REMARKS ON THE RELATION OF THESE LESIONS TO OTHER MORBID CONDITIONS OF THE NOSE AND THROAT.

BY JONATHAN WRIGHT, M.D.,
OF NEW YORK.

AN experience with such work extending over many years has long impressed me, and with an ever-increasing sense of its importance, with the great desirability that, connected with every large nose and throat clinic, a laboratory should be established in which all tissues removed from the patients should be systematically examined under the microscope. This should be done by a person thoroughly familiar with all the clinical problems presented by the histories, which in each case should accompany the specimen. Very meagre results are to be expected from the perfunctory examination of such material by a laboratory recluse. He should be in constant and thorough touch not only with all the phases of the morphological appearances of the tissue, but

[1] Read before the Laryngological Section of the New York Academy of Medicine, March 25, 1903.

with the clinical phenomena which accompany them. The endeavors of two sets of men, each only familiar with the clinical or the pathological side, however conscientious and earnest may be their labors, will always be, and have of necessity always been, markedly devoid of practical results in the advancement of our knowledge of the diseases of the nose and throat.

One tendency which is to be noted in all such work retards very much the elucidation of many of the most important problems we have to deal with, and that is the tendency to preserve for examination only the tissue from strange and unusual or doubtful cases, many laboring under the sad delusion that a malignant growth must of necessity furnish the most interesting tissue possible to the microscopist for study. Now, nothing can be more erroneous. In the study of the diseases which affect special regions of the body the examination of malignant growths microscopically is only of subsidiary interest. The problems connected with these belong more properly in the domain of general pathology. To a less extent this is true of the other two so-called "grand processes," syphilis and tuberculosis. The careful study of the common inflammatory processes and the connection of these with the benign growths is of very much greater importance. So multifarious are the appearances that, as is the case with the human physiognomy, no two specimens, no two sections, are exactly alike. Hardly any two pieces of tissue give the same reaction to reagents. Nay, more; one may almost say that hardly any two microscopic fields present the same appearance. This latter is especially true if we except the lymphoid tissue, whose hypertrophy presents more uniform pictures, due to the greater homogeneousness and regularity of the tissue, the slight changes to be observed from the normal, and the few elements involved. To the clinician anxious to know whether he has to do with cancer, syphilis, or tuberculosis of the nose or throat, the differentiation possible by the microscope is of the greatest importance and interest; but in studying the gradations between the different phases of manifest chronic inflammations and the more problematical steps to a papilloma or a fibroma this is of little service. The comparison of the appearances in a hypertrophic and an atrophic rhinitis and the study of their identical tissue changes is, in the present state of our positive knowledge, of much greater importance. The only way to arrive at a solution of many of these problems is by the patient and repeated study of every bit of tissue removed from the nose and throat in the routine of the clinic.

As an excuse for bringing before you to-night much repetition of what I have said on former occasions, I may plead the continuity of work along the same lines carried on for many years. As time has gone on new experiences have added somewhat to the links of the con-

tinuous chain which binds together many apparently dissimilar processes. To exhibit these properly it is necessary to repeat much which may appear old to you, in order to say only a little which may be new to any of you. It is otherwise impossible to make any advance in our knowledge of the correlation of morbid processes and their connection with normal conditions. After all, it is rather egregious vanity than commendable modesty to assume that what one has formerly said or written has not been forgotten. As to the continuous chain I have alluded to, it will, of course, be understood there are many links still missing. It will also be understood that there is very little, indeed, I have to offer you to-night which has not been presented by others.

(*a*) A RAPIDLY RECURRING "BLEEDING POLYP" OF THE SEPTUM NASI APPEARING TWICE IN A WOMAN, EACH TIME AT THE SEVENTH MONTH OF PREGNANCY.

These growths are to be classed among the angeiomata. There is no special reason for the classification of them in a separate category as bleeding polypi, a term which was inaugurated ten years ago by Schadewaldt, Alexander, Scheier and others.[1]

I find on looking at my records I have examined eight of these histologically. Any growth of the septum, benign or malignant, is usually very vascular—*e. g.*, the sarcomata—and one is frequently at a loss to be sure that the round-celled infiltration, which is always a prominent feature in such a growth as I show you to-night, does not warrant the diagnosis of small round-celled sarcoma. The subsequent clinical history is the only sure criterion, and frequent recurrences often cause the observer much anxiety as to the ultimate outcome.

A great deal of work has been done to illustrate the connection, both anatomically and clinically, between the erectile tissue of the sexual organs and that of the nose. As a very singular instance of it, I may report this case, which has been under my observation for a few years, in which a bleeding polyp appeared repeatedly in the nose of a woman at the seventh month of pregnancy:

A woman, aged twenty-five years, came to the Brooklyn Eye and Ear Hospital on September 17, 1901, with a history of the septum having been burned several years previously for obstruction. From this there resulted a perforation. She had since been married and was then seven months pregnant. Springing from the perforation in the septum was a round, vascular-looking growth attached to the inferior and posterior edge of it. It rapidly recurred after extirpation, and on examination at that time showed nothing but very vascular granulation tissue. Recurrence a second time was larger than ever. It was then more radically removed, bits of underlying cartilage being cut away with it. That specimen showed some disordered cell structure and was richer in blood-

[1] Archiv. für Laryngologie, Band i. p. 259 et seq.

vessels than the tissue at the first examination. It was supposed to be an ordinary bleeding polypus of the septum.

About one year later (November 26, 1902) the woman again came with the history that the growth had not recurred noticeably after the last removal, shortly followed by the delivery of her child, born at full term and healthy, nor did she notice any discomfort until she had again become seven months pregnant, when she returned with recurrence of the growth, which now sprang chiefly from the inferior border of the perforation. It was of almost exactly the same appearance as the previous ones. This was removed and rapidly recurred. On December 17, 1902, it was again removed, and Fig. 1 represents the histological appearances.

FIG. 1.

The microscopic appearances of a "bleeding polyp" of the septum, recurring twice at the seventh month of pregnancy. Photograph × 10 (retouched).

On microscopic examination the tissue is seen to be covered by degenerated flat epithelial cells, under which there is a layer of what appears to be hyaline degeneration of the connective tissue. The mass of the growth is made up of loose œdematous connective tissue in which there are a large number of mononuclear round cells which take the hæmatoxylon stain very deeply, and the whole growth is traversed by very numerous capillaries lined by a single layer of endothelium whose nuclei are very much swollen and project into the lumina of the blood-vessels. There is every evidence of considerable inflammatory action, but no proof of the malignant nature of the growth.[1]

Whatever the subsequent history of the case may be, the rapidity with which this vascular growth recurred during pregnancy and its

[1] Since this paper was written this patient has been seen several times, first about three weeks after delivery. The growth was then the size of a pea. A month later it was the size of a grain of wheat, and a third time, still diminishing. Apparently, therefore, the growth had already recurred and grown to considerable dimensions in the two months elapsing between the last removal and the birth of her last child, and in the two months which had succeeded delivery it was as rapidly disappearing.

quiescence or absence at other times is, in view of the previous literature, interesting to say the least. The coincidence of the appearance of this growth and its repeated recurrence at the seventh month of pregnancy is one of the clinical facts which, though they cannot be very lucidly accounted for, nevertheless, taken in the aggregate, point to a more or less important relationship between the nasal and the genital mucosa. In another publication I have shown the anatomical differences in the nasal erectile tissue of the bull and the steer.[1]

From anatomical as well as from pathological and physiological facts we know there is a more or less indefinite sympathy between the erectile tissue of the nose and the genitalia. In order to elaborate some considerations connected with this subject, I will quote rather extensively from some work I published seven or eight years ago:[2]

"In the erectile tissue of the nose the larger arterioles well supplied with muscular coats lie in the deepest layers of the mucous membrane close to the bone. They give off branches which supply, by a network of capillaries, the periosteum, the glands, and the epithelial layer of the mucous membrane. These capillaries are collected into the veins, which dilate into venous sinuses, the larger lacunæ of which are the deeper, the superficial lacunæ or "cortical network" communicating with them. These lacunæ again empty into the veins which accompany the primary arterioles into the periosteal layer.

"Zuckerkandl says he has never seen the arteries emptying directly into the venous sinuses. The same was said for a long time of the corpus cavernosum of the penis, but they were finally conclusively shown to do so, and I am not convinced that this does not occasionally take place in the erectile bodies of the nasal mucous membrane, though I have thus far been unable to trace the connection between the two.

"The capillaries, usually at least, do not empty directly into the venous sinuses nor into the radical veins accompanying the arteries. They are usually seen collected first into veins. The smaller veins of the periosteal layer empty directly into the radical veins accompanying the arterioles.

"Nevertheless, by comparing all these different conditions the probable mechanism of the blood-supply in the highly evolved nasal mucous membrane of man becomes pretty evident. The radical arteries and veins pass through various bony canals into the nose, as the large sphenopalatine foramen and smaller foramina in the ethmoid. The artery will evidently compress, when dilated, its accompanying vein against the bony walls, thus letting in more blood and limiting the outflow.

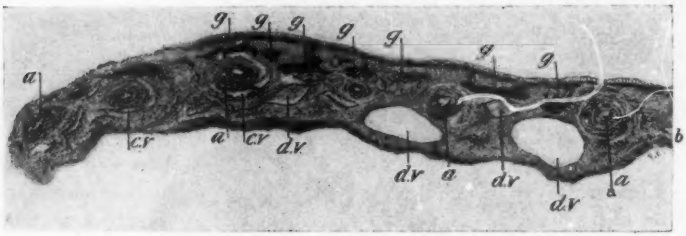
[1] New York Medical Journal, November 19, 1898.

[2] A Consideration of the Vascular Mechanism of the Nasal Mucous Membrane and its Relations to Certain Pathological Processes. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, May, 1895.

Contraction of the artery acts in the inverse sense. This arrangement has been described for the blood-supply of the marrow of the long bones.

"There is a similar mechanism, as the arterial branches with their veins lie in the deep or periosteal layer of the mucous membrane. Fig.

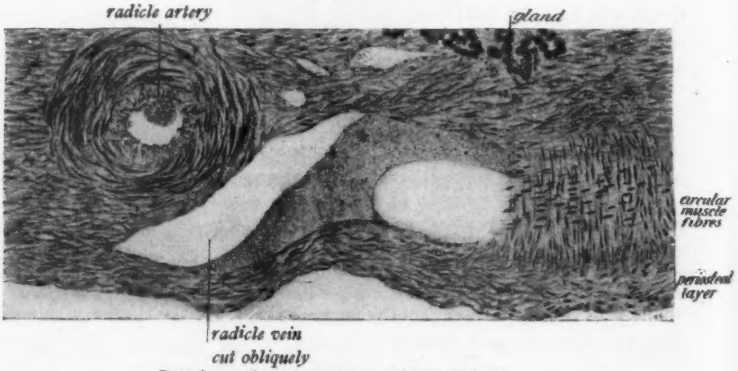
FIG. 2.



Nasal mucous membrane of sheep. *a*, artery. *b*, periosteal layer. *g*, gland. *d.v*, dilated vein. *c.v*, closed vein.

2 and Fig. 3 show very clearly how this occurs in the sheep. You will observe that many of the large veins lie between the very muscular arteries and the firm periosteum at the level of this particular section. Of the thirty or forty sections examined, this arrangement was evident

FIG. 3.



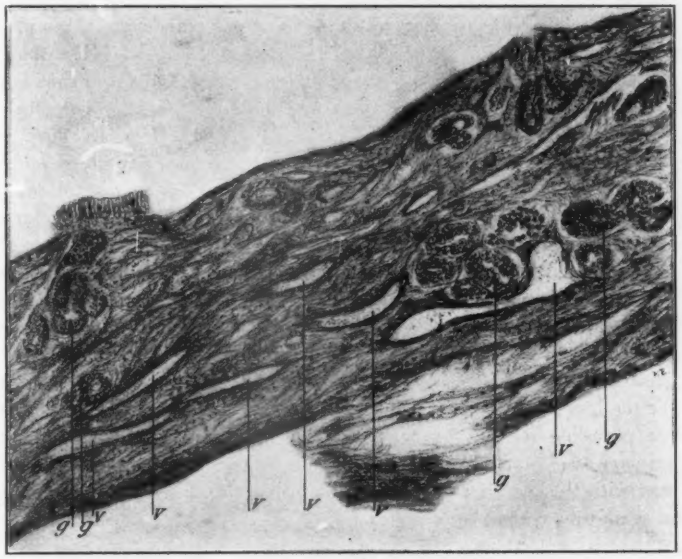
Deep layer of nasal mucous membrane of sheep.

in so many pairs that it is fair to presume that at some one or more points each radicle artery and vein stand in such a mutual relation that an increase in the diameter of the artery must result in an encroachment upon the lumen of the vein without entirely closing it. While this

drawing is from the mucous membrane of the sheep, the same arrangement, by careful study, will frequently be found in that of man (Fig. 4); but, owing to the very much more complex and irregular course of the vessels, it does not present such a striking and convincing illustration.

"There is such a complete anastomosis of the superficial veins with one another, with those of the skin at the edge of the nostrils, with the veins of the dura mater and of the orbit, that this obstruction to the venous return probably exerts its dilating tendency only or chiefly upon the

FIG. 4.



Nasal mucous membrane from septum of infant. *a*, periosteal layer. *v*, radicle vein. *g*, gland.

deep network of the erectile bodies. It does act, however, upon them as the supply and escape valve to the cavernous sinuses, and stands in the place of the muscles which compress the radicle veins of the penis and the clitoris."

Now this brings us to a point which is not sufficiently realized in nasal pathology. The nasal mucosa is a peculiar mucosa, differing essentially from all other mucosæ of the body in one very important particular. That is the presence immediately beneath it of bone structure in close relationship with its most important elements, the

bloodvessels and the glands. This is indicated at the level shown in the drawings by the periosteal layer. This relationship of the mucosa is still more peculiar in those thin lamellæ of bone, the turbinates, which are covered not on one side alone, but on both. I am obliged, however, to confess that I have not observed arterioles and veins in juxtaposition piercing these thin lamellæ through a common channel. As a rule they run parallel with these bony plates, and in the compression of the vein by the dilating artery, if they are a contributing part of the mechanism, they are non-elastic plates against which the compressible vein is apposed. This may be accomplished not only by the dilating artery, as I have hitherto urged, but by the contractile energy of the unstriped muscle fibres and the elastic fibres of the superimposed stroma. It is very probable indeed that compression of the glands also takes place and their contents are extruded by the same mechanism. Now this is the only mucosa in the body whose radicle bloodvessels are thus contained in dense unyielding channels, and the importance physiologically I have dwelt on in the extract I have just quoted. Not only must we bear this in mind when we consider the mechanism of the blood-supply of the mucosa, but it has an important bearing on our comprehension of various inflammatory processes. It doubtless is an important factor in the etiology of the unique lesion of atrophic rhinitis, and it probably is the cause of the frequency with which œdema supervenes in the chronic inflammation of the nasal mucous membrane, forming polypi or the so-called polypoid degenerations. We have œdematous polypi elsewhere, as for instance in the larynx, but the effusion of serum in growths elsewhere never reaches the degree observed in the nose. As for the lesion of atrophic rhinitis I quite agree with others that there are plausible reasons for believing that the essential lesion and the primary one in atrophic rhinitis is a bone lesion which interferes in some way with the radicle vessels which lie in bony canals, or are compressed in some way against bony plates.

(*b*) PAPILLARY ADENOMATOUS HYPERTROPHY OF THE MUCOUS MEMBRANE OF THE SEPTUM.

A number of years ago considerable discussion was elicited through the publication, by Dr. Hopman, of a large number of cases of what he called nasal papilloma, which many of us believed to be merely papillary hypertrophy of the mucous membrane of the nose, usually situated upon the inferior turbinated bones at their posterior borders, where we have regularly a large amount of erectile cavernous tissue. In several publications[1] I took the latter view with Chiari and many others. I believe it will now be conceded that this latter view has prevailed in nasal

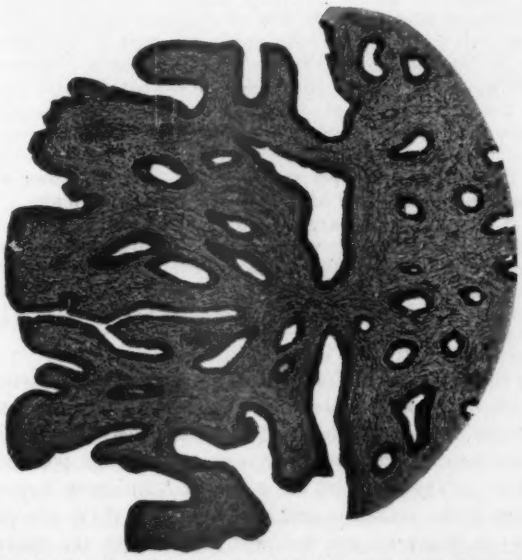
[1] New York Medical Journal, December 26, 1891; October 18, 1894; December 14, 1895.

pathology. While these papillary hypertrophies are usually found in the situation I have mentioned above, the following case will illustrate that the same form of growth may occur under certain conditions else-

FIG. 5.

The reduplication of the surface epithelium in a papillary adenomatous hypertrophy of the mucous membrane of the septum. Photograph × 10 (retouched).

FIG. 6.



The hyperplasia and reduplication of the glandular epithelium in a papillary adenomatous hypertrophy of the mucous membrane of the septum. Photograph × 10 (retouched).

where. From the drawing (Figs. 5 and 6) made under low power it will be plainly seen that we have to deal with the reduplication of the surface and glandular epithelium of the septum. The method by which this takes place I have explained in a paper on "Papillary Œdematous Nasal Polypi and Their Relation to Adenomata."[1] I am indebted to the kindness of Dr. W. F. Dudley for this specimen and for the following history:

Man, aged thirty-five years. He had had nasal polypi removed from both sides of the nostril. Ten years ago he had an abscess of the frontal sinus, which ruptured spontaneously. A surgeon had enlarged the external opening and curetted the sinus. Since then he had been treated for nasal polypi in both sides of the nose, and also in the frontal sinus. This specimen, "a thickening," was removed from the right side of the nasal septum, anterior third, at the junction of the triangular cartilage with the vomer. The thickening was in contact with the floor of the nose. There was no pain, no glandular involvement, and but moderate bleeding. There was some thickening also of the septum projecting into the left nasal cavity. As frequently happens in these growths, there has been some recurrence since the operation.

Microscopic examination shows under low power a very corrugated surface lined by a thin layer of columnar epithelium, giving it to the naked eye the appearance frequently seen in papillomata; but there is no real increase in the number of epithelial layers. The stroma is loose and œdematous, filled with mononuclear and a few multinuclear leucocytes, and a moderate number of capillary bloodvessels only slightly dilated, some of the walls being thickened in their fibrous coat, and the endothelium being usually swollen. The epithelium under the high power seems to be columnar in character, and there are in the sections a number of rings of epithelium, separated from the surface in the substance of the growth, evidently the walls of the acini of the hyperplastic racemose glands, cut transversely or obliquely. Some of these communicate with the depressions of the corrugated surface. The growth, except for the small number of bloodvessels, is very similar on its surface to those which are common at the posterior end of the inferior turbinated bones. The corrugation of the surface is largely due to the dilatation of the ducts of the glands, but also, I believe, to the lateral division of the surface columnar epithelial cells. The whole growth is to be looked upon as an exceptional instance, in the situation in which it was found, of œdematous papillary hypertrophy of the mucous membrane, which is becoming adenomatous.

During the preparation of this paper two specimens on the same day in sequence have come under my observation which illustrate some further points in the interrelation of these growths. Fig. 7 illustrates an ordinary papillary œdematous hypertrophy of the posterior end of the inferior turbinated body, the so-called "mulberry hypertrophy." Taking note of the unusually striking appearance of the dilated cavernous sinuses in this specimen, you will also observe the reduplication,

[1] New York Medical Journal, November 13, 1897.

the corrugation, or papillary condition of the surface. Now I believe that this epithelial hyperplasia is the essential one, and not the fibrous digitations which form the framework of it. At *a* I have had indicated somewhat schematically the condition of the racemose glands in this tissue. You will observe that there is relatively little change in these, saving some round-celled infiltration around them, the glandular epithelium being practically unaltered, and the lumina of the acini not being especially dilated. We may conjecture that the greater amount of fibrous tissue and the engorgement of the venous sinuses has by mechanical compression had something to do with the prevention of hyper-

FIG. 7.

The structure of the posterior end of the inferior turbinated body, showing the hyperplasia of the surface epithelium and the dilatation of the venous sinuses. The glands are unaffected, but are here much exaggerated in size to show their presence. Camera lucida × 10.

plastic changes in the glands at this point in this hypertrophy. This is not always the case in this locality, for, as you will see in some of the lantern slides I will exhibit, this glandular hyperplasia is present in other specimens from this locality where the sinuses are not so prominent, but the point is still better illustrated in the other specimen referred to above, which is a papillary œdematous hypertrophy of the posterior end of the *middle* turbinal. Here, in this case, we have no venous sinuses at all, and you may observe in Fig. 8 the involvement of the glandular epithelium as well as that of the surface. This is an unaltered camera lucida drawing, which sufficiently illustrates the

point. In the former specimen we have the papillary condition of the surface only, in the latter the papillary condition of the surface *and* the adenomatous hyperplasia.

These growths are rather uncommon in the nose at a stage of exclusive adenomatous hyperplasia, but are thus much more frequently found in the rectum, the uterus and its adnexa, and in the bladder. In the sections which I exhibit (see Figs. 5 and 6) in connection with this septum case I think you will be able to note the relationship not only of

FIG. 8.

The structure of the papillary œdematous hypertrophy of the posterior end of the middle turbinated body, showing the involvement of the glands. At *a* is seen the dilatation of a glandular duct helping to make the papillary surface. Camera lucida × 10.

the ordinary hypertrophies of the posterior ends of the turbinate to this growth, which borders on the class of adenomata, but you will see from the sections that we also have the marked œdema of the stroma, which is the only characteristic of the ordinary nasal polyp. Were it not for this lateral cleavage in the columnar epithelial cell leading to reduplications and inversions of the surface and glandular epithelium, we would call the hyperplasia by the clinical term polypoid. In studying these growths we must remember that embryologically the racemose glands of the mucosa are normally nothing but the inversions of the

surface epithelium, and we conceive of these adenomata as being nothing but the morbid activity of the cells excited by some stimulus, which we have every reason to believe is usually a chronic inflammation. Now, a very interesting and a very mysterious phenomenon is the frequency with which what you here perceive is essentially a benign growth becomes a malignant adenoma. When in these adenomatous growths you find areas in which the cells are multiplying not alone in such a manner as to form tortuous loops of epithelium of one or two layers, but so that there are many layers which intervene between the lumina of the false acini or loops of columnar cells and the stroma, we may suspect that the tumor is putting on a malignancy which, however frequent the recurrence may have been, has hitherto been absent. Hitherto we have had to do with a surface hyperplasia. When malignancy commences a deep destructive infiltration begins which we know will eventually develop into all the clinical and morphological characters of cancer.

It is a very plausible assumption and an entirely possible explanation to say that these benign hyperplasias of epithelium furnish the proper soil and a nidus for the specific contagium of cancer, and that when this tissue becomes the abiding place for it, then the infiltration begins. However attractive this theory may be, it lacks all the necessary elements of scientific demonstration. There is even not enough accumulation of circumstantial evidence to render the theory anything more than a suggestive possibility. This is not the place to enter into a discussion of the germ theory of cancer. Recent investigation has fully demonstrated the unsatisfactory character of the evidence thus far presented, but we must remember that nothing has thus far been advanced to demolish the theory. It seems probable that we must await the development of higher resolving powers for our microscopes and for more sensitive chemical reagents, but we should also keep our minds in a more receptive condition as to the possibility of the independent existence of simpler entities than the animal cell. That is no longer a microcosm. It is a macrocosm. For a long time various morphological phenomena within the cell have been studied under the high powers of the microscope, and recently the astounding facts which have been elicited in the laboratory study of immunity have excited the minds of investigators to such an extent that already theories have been advanced to explain them, which future fuller knowledge is very likely to demonstrate as erroneous, or at least as premature. These are the chemico-biological aspects of the problem of intracellular life which are apt to be proven hereafter to have a decided relationship to the etiology of cancer.

(c) A CYST IN THE LYMPHOID TISSUE OF THE PHARYNX.

From time to time, for many years, I have been much interested in certain forms of cystic growths found in the nose and throat.[1] The retention cysts which form in the racemose glands are common enough[2] and well enough understood to deprive them of any special interest when found. Only less so are the so-called inclusion cysts, such as we meet with in the pharyngeal vault, called by Tornwaldt the pharyngeal bursa, being merely the space included by the agglutination of two contiguous folds of the mucous membrane. I have also met with this formation along the lateral walls of the pharynx.[3] It occasionally happens—at least I have once observed it—in the posterior ends of the inferior turbinated bodies when enormously hypertrophied, that the dilatation of one of the cavernous sinuses assumes the size of a cyst filled with blood. Besides this, the cysts forming in nasal polypi are not always due to the dilatation of glands which may be contained in the pendent tissue, but in rapidly forming polypi, and especially in those exceptional cases where the patient is younger than sixteen or seventeen years, are found cysts formed by the breaking down of the scanty stroma and the more abundant coagulated fibrin which goes to make up the framework of the polyp. Elsewhere I have drawn attention to this method of cyst formation as being allied to the formation of blebs by the effusion of serum just beneath the epithelium, this being frequently of neurotic origin.[4] But there is another form of cyst which is very rarely met with and always, of course, in the pharynx, and that is one formed *within* the structure of the lymphoid tissue. It results apparently from the dilatation of one or more of the lymph spaces through some cause which I cannot fully understand, as it would seem that impediment to the lymphatic circulation could hardly be so localized as to cause dilatation of the channels behind it. Whatever may be the cause, however, it is a fact that these cysts are occasionally met with. In the drawing Fig. 9, herewith produced from a section of a specimen kindly furnished me by Dr. Berens, this is especially well seen. It came from the glosso-epiglottic fossa. Apparently several contiguous microscopic lymph nodes embedded in the loose connective tissue were the seat of this method of cyst formation. In the drawing, at the larger end, may be seen a lymph node of which almost the entire calibre is taken up by the dilated lymph space, there being merely a rim of lymphoid tissue around the cavity. At the small end may be

[1] A Cyst of the Pharyngeal Bursa. Medical News, September 7, 1889.

[2] Some Remarks on the Structure of Œdematous Nasal Polypi. New York Medical Journal, November 4, 1893.

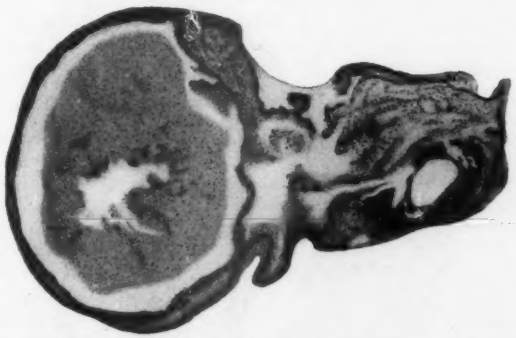
[3] A Cyst of the Nasopharynx and a Cyst of the Oropharynx. New York Medical Journal, 1895.

[4] Remarks on the Etiology of Nasal Polypi. Laryngoscope, 1899.

seen the beginning of another cyst which is forming in this manner, the encircling rim of the lymphoid tissue in this last case being relatively much larger than that of the cavity at the larger end. The case had no especially marked clinical history, except that of slight irritation of the throat.

There is some tendency to confound these rare cysts with the equally rare cases of abscess of the lymphoid tissue, and these two again with the retention plugs found in the lacunæ of the tonsil which have been sealed over in the process of inflammation. In the cases of true abscess,

FIG. 9.



Showing at the larger end of the drawing a lymph node whose area is almost completely occupied by a cavity lined neither by epithelial nor endothelial cells, but connected directly with the lymphoid tissue, while at the smaller end a similar cavity is observed with a thicker rim of lymphoid tissue. Photograph × 10 (retouched).

zones of inflammation and colonies of cocci, presumably pathogenic, may be found in the neighboring lymphoid tissue which has not yet broken down into an abscess cavity. In the retention cysts of the lacunæ we find either a complete coating of epithelium on the walls or a plainly recognizable remnant of it. In this specimen neither of these conditions are present and we have, I believe, a true lymphatic cyst.

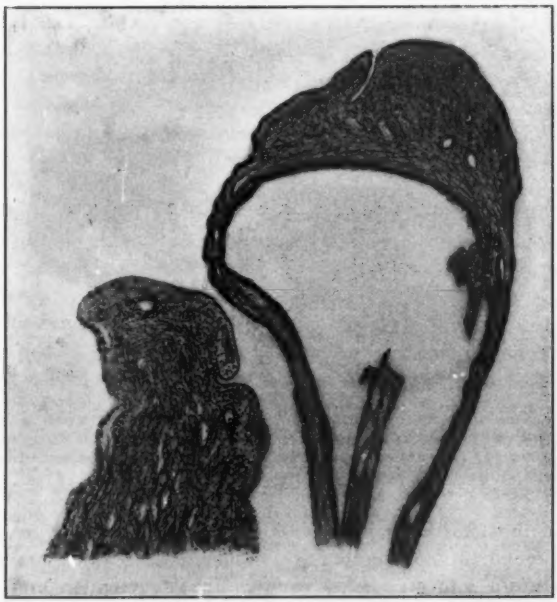
(*d*) EFFUSION OF SERUM INTO THE NASAL MUCOSA IN CORYZA.

Besides the cases of dilated spaces within morbid growths which I have mentioned and which are properly designated as cysts, we have in acute coryza, especially when affecting the already œdematous mucosa of the nose, a dilatation of the lymph spaces due to the sudden and excessive exudation of serum from the bloodvessels into the stroma weakened in the processes of chronic inflammation. This is illustrated in the drawing Fig. 10, taken from a section of the mucosa of a middle

turbinated body removed during the period of a coryza when the nasal passages are most completely occluded.

In a mucosa not too much altered by chronic inflammation there is still contractile power enough in the unstriped muscle fibres and in the elastic fibres of the stroma to temporarily drive out the blood during the attack from time to time, and, finally, on the subsidence of the

FIG. 10.



The dilatation of a lymph space or the separation of the fibres of the stroma of the nasal mucosa by the effusion of serum during the congestive stage of a severe coryza. Dimensions: 6 x 3 mm. Camera lucida × 10.

coryza to permanently squeeze out or cause the absorption of the serum. In a mucosa badly damaged as to the contractile energy of these elastic and muscle fibres, this ability of the mucosa to regain its normal volume temporarily and permanently is weakened, or has entirely disappeared in exact proportion to the amout of damage done by the previous long-standing chronic inflammation.

REVIEWS.

APPLIED SURGICAL ANATOMY REGIONALLY PRESENTED, FOR THE USE OF STUDENTS AND PRACTITIONERS OF MEDICINE. By GEORGE WOOLSEY, A.B., M.D., Professor of Anatomy and Clinical Surgery in the Cornell University Medical College; Surgeon to Bellevue Hospital, etc. Octavo, 511 pages, with 125 illustrations, including 59 full-page insert plates in black and colors. Philadelphia and New York: Lea Brothers & Co., 1902.

A CAREFUL examination of Dr. Woolsey's new book makes one feel that he has made an addition to medical literature of genuine value. Not that there is anything particularly new in surgical anatomy, and not that the author has more than kept pace with the advances of operative surgery, but it is a happy union of fact and practice, the latter based upon the former, which brings into distinct view the enhanced advantage that can be taken of this combination. The book bristles with good advice about many minor as well as more important essentials, and it is withal so entertainingly written that such advice is made to appear doubly welcome.

To speak more definitely of particular portions, we are tempted to criticise the rather meagre details which are given under the head of localization of cerebral functions. Surely a surgeon like the author might have described the method of Chiene, or the cyrtometer of Wilson, without stepping aside from his expressed intention, inasmuch as other and perhaps less simple methods of locating the principal fissures are given. An excellent instance of the applied anatomical method of diagnosis is afforded by the description of facial paralysis under the head of nerves of the head and neck. Mention is made of the anterior method of attack upon Meckel's ganglion, but not of the approach after lifting the zygoma. In the description of the nasopharynx, the anatomical arrangement of its adenoid tissue is briefly given, but the author has omitted to call attention to the fact that originally it forms a perfect collar of lymphoid tissue around the neck of an embryonic canal. He has made the same omission, by the way, in describing the appendix, whose origin from the cæcum is similarly arranged. These facts are of importance, because such tissue is extremely prone to succumb easily to infectious processes, which will explain the local disaster often seen in the throat and about the appendix.

His description of the cervical sympathetics is brief and not so full as one might wish, especially in view of the growing importance attaching to these nerve trunks and ganglia, in view of possible surgical attack upon them for at least three more or less common conditions. The writer does not like to complain of omissions, and yet he regards this book so highly that he would like to see it so complete and perfect in

all its parts that one need not refer to any other work upon its general subject.

The description of the cervical fasciæ, their various planes and compartments, is excellent and of great practical importance. When describing the branchial arches the author speaks of the first as forming the upper jaw, which is not our understanding of the embryology of the jaw. In his description of the thorax and of the roots of the lungs we would have been glad to see more space given to Bryant's well-devised and well-described operation for their exposure from behind, of which the reader would get no adequate idea from this source. So, too, in dealing with the heart, the author speaks of wounds of its various parts and of the possibility of their treatment by operation, but gives no description of any method by which the heart can be exposed for the purpose. Considering the richness of his advice in most other instances, this would appear to be a distinct omission. In speaking of the abdomen, a section of great value is that dealing with "Operations and Incisions," and here the author is as full as could be desired. This is true also of hernia operations, where the question is asked, How are we to recognize the different hernial layers? and then answered in a very satisfactory way; the author replying that it is neither necessary nor always possible to distinguish all of them, but showing how those which are distinct can be identified. In the surgical anatomy of the lumbar region are found some excellent data concerning psoas and iliac abscesses, it being shown that there are at least two well-marked forms of the latter.

As would be expected, the anatomy and the relations of the appendix are well discussed with the single exception above noted. An example of the minuteness with which particular points are treated may be found in the paragraph devoted to the nerves of the liver, where is furnished an explanation for the occurrence of pain over the right shoulder in certain cases of hepatic disease. The section on the pancreas is disappointingly short. Surely, its surgery has now attained sufficient importance to justify a more complete description of the methods of approach and of affecting posterior drainage. He who would acquaint himself with this subject would turn in vain to this work for that which he should find there. The explanation of retroperitoneal hernia is very good and more succinct than can be found in the same space in any other work with which we are familiar.

And so one might go through this book, finding no fault except here and there where it fails to contain something which the reader might expect to find in it; but it is a book of remarkable merit, showing not merely a large amount of research, but the happy faculty of giving to each anatomical fact its value when applied in practice. The work is sufficiently though not luxuriously illustrated.

Most of the illustrations have been furnished by French works more or less familiar to American students. They are probably just as good as any which might have been made from original sources; they seem, however, to detract from the distinctly American character of the work. We are pleased to see that Dr. Woolsey has abandoned the old expression lymph glands, and adopted the only term which should ever be used—*i. e.*, lymph nodes. The term gland applied to these structures has always been misleading, and implies a primary conception of their function which is quite inaccurate.

The value of the work could be much enhanced by a more complete index. For instance, we find on Plate IX., p. 124, an allusion to the glands of Webber and Blandin, of which we fail to find any description in the text, and to which there is no reference in the index. If they are worthy of mention in the plate they certainly deserve some allusion elsewhere. In spite of these trifling failures or faults, the mention of which might almost be considered captious criticism, we have formed a very high estimate of the value of the work, which we believe to be of very great value alike to general practitioners and to specialists.

R. P.

A GUIDE TO THE PRACTICAL EXAMINATION OF URINE, FOR THE USE OF PHYSICIANS AND STUDENTS. By JAMES TYSON, M.D. Tenth edition, revised and corrected, with a colored plate and wood engravings. Philadelphia: P. Blakiston's Son & Co., 1902.

THE present is the tenth edition of this excellent little manual, and, although new matter has been added, the book has been so revised that its size is not greatly altered. The introduction treats of the technique of urine examination and the general physical and chemical characters of urine. The necessary apparatus for these determinations is described, and all the important chemical tests, together with the reagents used, clearly and concisely given. Part II. deals with the urinary sediments. The text is fully illustrated by woodcuts, both organized and unorganized sediments being adequately pictured. In Part III. methods for the determination of urinary calculi are given, and in an appendix most useful tables are added for reducing the metric system into the English, and *vice versa*. Altogether, the book forms a most excellent guide to the subject of urinalysis, and is especially adapted to those wishing a practical knowledge of urine examination from a clinical standpoint.

W. T. L.

THE ELEMENTS OF BACTERIOLOGICAL TECHNIQUE: A LABORATORY GUIDE FOR THE MEDICAL, DENTAL, AND TECHNICAL STUDENT. By J. W. H. EYRE, M.D., F.R.S. Edin., with 170 illustrations. Philadelphia and London: W. B. Saunders & Co., 1902.

WITH the general adoption of bacteriological investigation as an aid to diagnosis in clinical medicine, and the widespread use of bacteriology in various branches of industry, there results a definite need for a book devoted exclusively to the technique of this side of scientific work. The present book is not especially intended for the student of medicine, but deals with the methods of bacteriological investigation from a much broader aspect than is to be found in the usual text-books on pathological technique. Indeed, only a very small portion of the volume is allotted to the study of pathogenic bacteria, and thus the work is adapted for use in the dairy or brewery as well as in the pathological laboratory. The first portion includes detailed descriptions of the necessary glass apparatus, microscopes, incubators, the principles of sterilization, and general examination of bacteria and other micro-fungi.

Bacterial stains and the preparation of nutrient media are fully

recounted, and one chapter is devoted to the identification of bacteria, including both physiological and chemical examinations. A classification of fungi, with a description of the anatomy and physiology of the schizomycetes, is a useful addition. At times the description of apparatus and their use impresses one as being unnecessarily detailed, although this is scarcely a fault in a book dealing with the elements of a subject. On the other hand, the portion devoted to the study of the pathogenic bacteria only suggests certain lines of investigation, and would be of little avail to one unfamiliar with the subject.

It is also to be regretted that some of the special media recently devised for the identification of the typhoid bacillus have been omitted, especially since the separation of the colon bacillus from the typhoid bacillus is dwelt on at some length in the chapter on Water-examination. Altogether the book is valuable, since it comprises the standard and most useful method of general bacteriological investigations. The volume numbers something over 350 pages, and contains numerous cuts which amply illustrate the text. W. T. L.

ANLEITUNG ZUR DIAGNOSE UND THERAPIE DER KEHLKOPH-, NASEN-, UND OHRENKRANKHEITEN. Vorlesungen gehalten in Fortbildungscursen für practische Aerzte, von DR. RICHARD KAYSER, in Breslau. Berlin: Verlag Von S. Karger, 1903.

THIS little book of 170 pages is one of the most practical guides to diagnosis and treatment of the more ordinary pathological conditions met with in the nose, throat, and ear which it has been our pleasure to read. It is intended for the use of the student, the general practitioner, and the beginner in the specialties with which it deals, and within these limits it is a very complete exposition of them. Its author is to be congratulated upon the wisdom with which he has pointed out those conditions which may be properly treated by the tyro as distinguished from those which require special skill in their management. The illustrations are well chosen, accurate, and graphic. F. R. P.

THE MATTISON METHOD IN MORPHINISM. By T. B. MATTISON, M.D., Medical Director, Brooklyn Home for Narcotic Inebriates. Pp. vi., 40. New York: E. B. Treat & Co., 1902.

A PHYSICIAN who can sum up the results of thirty years' experience in less than forty pages should attract our attention. In this little book he presents a modern and humane treatment of the morphine disease, consisting in preliminary sedation by sodium bromide, rapid deprivation of the drug, meeting the reflex symptoms mainly with codeine, combating the insomnia by trional, and making use of various agencies for the relief of disquieting symptoms. The book is a strong plea for humane treatment, safeguarded against deception and likelihood of relapse, written in a popular style; also, at the same time, sufficiently explicit for the practitioner having the facilities to successfully follow.

R. W. W.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Metabolism in Albuminuria.—EMERSON (*The Johns Hopkins Hospital Reports*, vol. x. p. 323) has made a very careful study of the disturbances of metabolism in a preliminary series of ten cases of nephritis in the medical wards of the Johns Hopkins Hospital. The work was undertaken with the view of determining, if possible, some of the influences governing the amount of albumin in the urine of these cases. The albumin and nitrogen excretion in the urine were specially studied. The former was estimated gravimetrically, and the latter by the Kjeldahl method. Some of the cases are illustrated by charts, indicating the curves representing the total urine, albumin, nitrogen, and temperature lines. His conclusions, with some additional details, are as follows:

1. The percentage of albumin is the best index for the course of a case of albuminuria.

2. In many cases of chronic nephritis there is an acute process in progress, and it is this latter which governs the course of the disease. Variations in the course of this acute process are shown by (*a*) increase in albumin per cent.; (*b*) slight rises in temperature.

3. The effect of various diets, therapeutic measures, muscular work, etc., on the albuminuria is often produced by their effect on this acute process.

4. In governing the diet in nephritis, slight rises in temperature should be taken as evidence that the diet is unsuited to the case.

5. While the acute process is active, milk is the best diet; not too much, and properly diluted. After the acute process has subsided, the patient may even benefit from additions of bread and butter, rice, fruit, or even, later, of meat.

6. If the day and night urines be studied separately, it was found that (*a*) the line of water excretion for the day is practically parallel to that of the

night; but the changes in the night preceding gives the curves the appearance of being the reverse of each other; (*b*) the albumin per cent. of day urine is practically always above that of the night; (*c*) in the night urine the albumin and nitrogen lines are practically parallel, showing some definite relation between the excretion of these, and the percentage of each varies inversely as the amount of urine to a certain degree.

Under normal conditions the kidneys, as well as the other organs, rest somewhat during the night. Quincke, Iljisch, and Laspeyres drew attention to some interesting changes occurring in disease. Iljisch found that in liver, kidney, and heart diseases which produce œdema, the urine voided per hour during the night contains more solids and is greater in amount than that during the day. In renal diseases, even though no œdema be present, the above is true. Laspeyres studied this point in a good many heart, renal, and other diseases. It was confirmed in certain cases of nephritis. He found it true in certain cases with cardiac or arterial disease, and in acute nephritis or chronic parenchymatous nephritis without heart lesion, the normal ratio obtained. He considers, therefore, that this abnormal ratio depends on the organic circulatory disease, and not on the renal condition alone. His explanation is essentially that of Quincke's, that during the night the kidneys have a chance to excrete the fluid of which during the day the tissues could not rid themselves owing to the circulatory disturbances.

On the Micrococcus of Acute Rheumatism.—E. W. AINLEY WALKER (*The Practitioner*, February, 1903, p. 185) advances bacteriological evidence which, with that of other investigators previously published, tends to strongly support the view that there is a specific organism that causes rheumatic fever.

Of the various organisms that have been isolated in cases of rheumatic fever, staphylococci and streptococci were the ones that were most frequently isolated by the earliest investigators. Achalme isolated a bacillus which gave positive results in experiments on animals. Recently much attention has been directed to an organism which was described by Apert and Triboulet in 1898, but which is, possibly, identical with that isolated by Popoff in 1887. Poynton and Paine have, up to the present time, obtained this diplococcus, as they prefer to consider it, from eighteen cases of acute rheumatism, and have by its inoculation into animals produced polyarthritis, pericarditis, myocarditis, endocarditis, pleurisy, nodule-formation, fungating endocarditis with visceral infarctions, and probably chorea. Fritz Meyer has supported their results in Germany. Poynton and Paine regarded this organism as the specific cause of acute rheumatism, and called it the diplococcus rheumaticus.

Walker and Beaton took up the bacteriological investigation of rheumatic fever, and they have come to the conclusion previously expressed by Poynton and Payne, that a particular micro-organism, and no other, is constantly associated with acute rheumatic lesions. They have isolated this micro-organism in fifteen rheumatic patients. These comprised eight cases of acute rheumatism, three cases of chorea in children, and four of malignant endocarditis in rheumatic subjects. By inoculation of the organism into rabbits they have produced the following effects: acute septicæmia, pericarditis, endocarditis with beady vegetations, pleurisy, and monarthritis or polyarthritis. The

organism has been found in pure culture in the blood, in all the lesions, and in the urine of inoculated animals. Although Poynton and Paine admitted that their organism sometimes formed chains, yet they preferred to call it a diplococcus. Walker and Beaton, however, rather regard it as a form of streptococcus, and suggest micrococcus rheumaticus as a more suitable name for it.

Is rheumatism a manifestation of an attenuated streptococcus septicæmia, as Gustav Singer strongly holds, or is it due to a specific organism? Walker and Beaton, while admitting that it has not yet been definitely established, support the latter view. Specificity, they say, can only be established by the eventual discovery of some characteristic difference, either in the micro-organism or its products, sufficient to distinguish it with certainty from the other members of the "streptococcus" group. They have found some proof to support the view that the organism is a specific one. Marmorek claimed to have proved the identity of all streptococci in man—with the possible exception of that of scarlet fever—by the observation that they all refuse to grow in filtered culture-fluid in which streptococcus has been previously grown and filtered out, although other organisms can grow in such media. Walker and Beaton tested two cultures of their micrococcus rheumaticus by the application of this method, and found abundant growth occurring in the inoculated fluids. They feel that the bacteriological study of rheumatic fever has now reached the stage when some hope of securing a curative serum may reasonably hold out.

SURGERY.

UNDER THE CHARGE OF

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On Four Cases of Perforating Gastric Ulcer, of which Three Recovered.—JONES (*British Medical Journal*, November 29, 1902), after reporting his cases in detail, states that the first case was as simple as the second was complex. A fairly movable ulcer, localized extravasation, and immediate operation were enough to ensure success. The second case, which died, was under chloroform for fifty minutes in consequence of adhesions which had to be separated and the involvement of the cardiac end, the fixation of which rendered suturing a matter of considerable difficulty. This patient died on the fourteenth day after the operation, and at the autopsy a large abscess cavity was found near the posterior portion of the under surface of

the diaphragm. There was a perforation through the diaphragm and into the left lung. Further examination showed the ulcer to be completely healed. Both the last cases were very encouraging, the third inasmuch as operation was not performed until fourteen hours after the rupture had occurred. Although leakage had occurred in the last case, the stomach contents did not appear to be of a very irritating kind. A subphrenic abscess is often found in those cases where the perforation is of the anterior wall of the stomach, and this may be accounted for in either one of two ways: 1. By direct trickling of septic material through the foramen of Winston. 2. By lymphatic absorption. In regard to operative technique, it is well in all cases to scrape the surfaces and edges of the ulcer, and when practical to use a purse-string suture as a preliminary measure. This can be done in a few seconds and all extravasation stopped while the final occlusion is completed. Dry dabs should supersede irrigation, which serves to dilute, disseminate, and make more soluble the toxic contents. As Turner has suggested, one can easily infect the lesser peritoneal cavity by irrigation of the greater. Tobin has stated that no case of perforated gastric ulcer should be removed from where the union has occurred, for any motion simply aids in the escape of the stomach contents into the peritoneal cavity.

Operations for Gastric Ulcer, Acute and Chronic.—PARKER (*British Medical Journal*, November 29, 1902) states that he operated on five cases of chronic ulceration with sudden perforation, with the result that four made a complete recovery, and one died thirteen and one-half hours after operation. In a second series of four cases of chronic ulceration with slow perforation, or, in other words, when the chronic ulceration was attended with a destructive process, but without extravasation, two died and two recovered. In the fatal cases the stitches in each case gave way on the fifth day after the operation. In one case exhaustion was the cause of death, while in the other it was due to a purulent peritonitis.

A Clinical Lecture on Some Cases Simulating Acute Appendicitis.—BARKER (*British Medical Journal*, February 28, 1903) states that the conditions closely simulating appendicitis are: (1) ruptured pyosalpinx; (2) ovarian cyst strangled by twisted pedicle; (3) twist and strangulation of omentum; (4) perforated gastric ulcer; (5) retrocæcal hernia; (6) broken-down caseating glands; (7) ileocæcal cancer, with abscess; (8) hæmatoma of broad ligament; (9) reduction of hernia en masse; (10) intussusception. Ovarian cyst, strangled by a twisted pedicle, may present typical symptoms of the acute form of appendicitis. In fact, in two such cases under the author's care the correct diagnosis was only made after the abdomen was opened. In a recent case of twist and strangulation of the omentum the patient gave a history and presented symptoms wonderfully like those of acute appendicitis—onset, with sudden pain in the right groin, vomiting, abdominal distention, a tender lump above Poupart's ligament, and elevation of temperature. The diagnosis was only made on operation, which exposed the real cause of the trouble. In one case a perforated gastric ulcer gave the symptoms of appendicitis: Sudden onset of pain in the right iliac fossa, which later became general throughout the abdomen. Tenderness and

rigidity of the abdominal walls, slight absence of resonance in the right flank, vomiting, and a rise of temperature to 100° F. There was no shock. The patient also had a reducible right inguinal hernia, which she had reduced on getting into bed, and the first thought was that it had gone back en masse, but there were no definite symptoms. Laparotomy settled the diagnosis, and the patient made a rapid recovery. In one case a retrocæcal hernia closely simulated appendicitis, but the operation showed a gangrenous intestine and general peritonitis, which was soon followed by death. Broken-down caseating glands in the right iliac fossa simulating a subacute appendicitis is not an uncommon condition. In one such case the temperature was up and down; there was a diffused swelling in the right iliac fossa, which was not very painful. On operation a chain of caseating glands running from the cæcum through the mesentery was found and removed and the patient recovered. Although ileocæcal carcinoma with abscess is an uncommon condition in one case of the author's, there was a ring of cancer in the valve, a perforation and resulting abscess, and so all the symptoms of appendicitis. More rarely hæmatoma of the broad ligament, reduction of a hernia en masse, and intussusception may simulate appendicitis, but in the last condition the differential diagnosis should be comparatively easy.

Hydatid Costal Cysts.—GÉRAUD and MIGNOT (*Revue de Chir.*, No. 1, 1903), after reporting in detail the results of operation in one case, state that the hydatid cysts of bone during a long period of their evolution are of small size and remain latent. It is not the same when they have destroyed a portion of the bone or have extended to the outside. They then present two important symptoms: the spontaneous breaking of the tumor and swelling. This breaking is the result of any insignificant traumatism during any sudden movement, and is often the first symptom revealing the presence of the hydatid disease. More frequently, however, it is the swelling which first attracts the attention. This swelling is smooth, hard, or of unequal consistence, often giving the sensation of parchment crepitation; soft, depressible, presenting rarely the special fremitus, when the hydatids have extended out of the bone and are spread throughout the neighboring soft tissues. Occasionally this tumor is reducible in the interior of the bone; occasionally also when compressed alternately by both hands the two extremities often may give to the contents a movement of coming and going, due to the passage of the mass under a point of bone, as was noticed in the author's case. As the tumor grows it encroaches upon the skin, which is susceptible of being infected, and then abscess formation, which either opens spontaneously or demands an incision for its relief. These infections are very serious and perhaps fatal, and are often the result of an infection developing in a bone affected with cystic degeneration. The phenomena due to the compression of the nerve trunks of the brain or the cord may add to the symptoms those of neuralgia, paraplegia, or the symptoms of a brain tumor, but they present no special characteristics other than those appertaining to all tumors of the bones, the brain, or the spine. One very rarely makes the diagnosis of hydatid bone cyst, and more often the condition is unperceived until the spontaneous fracture of the affected bone attracts the attention. Then one should also think that the spontaneous fracture may be due to tabes, gummatous

osteomyelitis, or sarcoma. The fracture due to tabes is so recognized by the other signs of this condition, the gummatous osteomyelitis by the history of syphilis, the osteocopic pains, and, contrary to the hydatid disease, recovery will follow immobilization, the sarcoma develops rapidly, is accompanied by local heat, by a subcutaneous network of veins more developed than on the opposite side, and sometimes by the movement of pulsation when the tumor is very vascular. Outside of this accident the affection is marked by a swelling of slow and torpid evolution, and should be differentiated from osteosarcoma, and, above all, from tubercular osteitis, which present a clinical picture closely resembling that of the hydatid cyst of bone. However, the tension of the tumor produced by the first affection is much less than that of the second, which gives the sensation of a very stiff and resistant packet. It is certain that the diagnosis is very difficult, and that one is more apt to make the diagnosis of a cold tubercular abscess than that of hydatid cyst. The best method of diagnosis is by capillary puncture or incision, which has the advantage of being provided for at the first for a radical operation. The treatment is surgical, for the indication is to remove all of the hydatid vesicles without their breaking, and so prevent a secondary infection. One difficulty that may present itself is the difficulty of evacuation in those cases where the medullary canal of a long bone or the body of a vertebra is involved. In order to facilitate this search and so absolutely clear out the region infected with the vesicles, it is necessary to make a long incision and then trephine the affected bone and then to hollow out until healthy bone is reached. All the infected bone should be removed either with a gouge or a curette, and then the resulting cavity thoroughly sponged out with salt solution and sterile pads. The depression which results from this loss of substance should be drained, and if suppuration has taken place in the cysts the wound should be left freely open, as after trephining for osteomyelitis. In the case of hydatid cysts which develop in a rib, the indication is to do a partial resection of the bone, as was done in the author's case, care being taken to go wide of the area of disease. If one does not resect enough, one invites a return of the condition. The same operative measures are indicated for the lesions of the bones of the members, lesions which otherwise necessitate amputation, particularly in the case of the lower limb.

A Simple Method of Operating on Piles.—MITCHELL (*British Medical Journal*, February 28, 1903) states that he has used this method with success during the past four years. The technique consists in dilatation of the sphincter, which will bring the piles fully into view, and then the mucous membrane is sponged with a 1:1000 solution of bichloride of mercury. A pile is then clamped in a long, narrow-bladed forceps, such as Kocher's artery forceps. The redundant mucous membrane and pile are cut away with scissors. A curved needle, threaded with catgut that has been hardened in formalin, is then inserted immediately above the clamp and the end of the catgut secured by a knot. A continuous suture is rapidly applied around the clamp, which is then withdrawn and the suture tightened, leaving a vertical line of continuous suture within the rectum. Each pile is similarly treated in turn. The advantages of this method are its rapidity and the lack of bleeding. The suture being continuous is an efficient hæmo-

static. After the forceps are withdrawn it cannot possibly slip, so there is no danger of secondary hemorrhage; no raw surfaces being left, the bowels are encouraged to act regularly from the first. As a rule, patients are able to be up in about a week. The catgut, being absorbed in eight or ten days, does not require removal.

THERAPEUTICS

UNDER THE CHARGE OF

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Intravascular Antisepsis.—DR. J. M. FORTESQUE-BRICKDALE gives the results of a number of experiments conducted at the Jenner Institute of Preventive Medicine. In planning the experiments he had two objects in view: first, to test the toxicity of various antiseptics when injected into the veins of rabbits, and, second, to discover if any of them exerted any influence on the course of an artificially induced septicæmia. In the first series the following substances were chosen: mercury perchloride, mercury oxycyanide, formaldehyde, chinosol, a mixture of formaldehyde and chinosol, protargol, and sodium taurocholate. The conclusions he drew from this series of experiments were: (1) mercury perchloride, mercury oxycyanide, and protargol cannot be injected intravenously into rabbits in sufficient strength to produce an antiseptic effect lasting over several days; (2) that a mixture of chinosol and formaldehyde is too toxic, even in minute doses, to be of use for practical purposes; (3) that chinosol or formaldehyde can be injected intravenously so as to produce a solution which would have an inhibitory action *in vitro;* (4) that sodium taurocholate can be injected in small doses, but the toxic effects manifest themselves after a few days. In the second series made to determine the effect of these antiseptic solutions on anthrax infection, the following conclusions were drawn by the author: (1) that rabbits injected daily with non-toxic doses of mercury oxycyanide, formaldehyde, chinosol, protargol, or mercury perchloride are not thereby protected from the usual effects of previous inoculations of virulent anthrax; and (2) that chinosol and formaldehyde in large doses so depress rabbits infected with pneumococcus that they die sooner than untreated animals. He concludes that at the present time there is no experimental evidence which would warrant the assumption that the course of septicæmia in animals can be influenced favorably by the intravenous injection of antiseptic substances, and that the only result to be obtained by pressing such treatment beyond the maximum non-toxic dose is to hasten the death of the animal.—*The Lancet*, 1903, No. 4141, p. 98.

The Treatment of Typhoid Fever by Acetozone.—Dr. F. G. HARRIS has tried this remedy in 128 instances of typhoid fever in the Cook County Hospital, taking advantage of a recent epidemic of typhoid, during which at least 600 patients with typhoid fever were admitted to the wards between July 1 and November 1, 1902. The cases were not selected ones and special wards were set apart for giving the acetozone treatment. As is well known, acetozone was first prepared by Novy, and its action is similar to that of hydrogen dioxide, save that it gives off more active oxygen than the former compound; but while giving off more active oxygen, it does not do so with the same violence and rapidity as is observed with hydrogen dioxide. This drug was administered in solution which contained 12 to 15 grains of the powdered acetozone to a quart of hot water. This is placed in a bottle which is stoppered and vigorously shaken from three to five minutes. It is then set aside to cool, and is kept in the form of one-half-gallon bottles in a refrigerator. The solution is used to replace water and all other liquids except milk, which is practically the entire food used during the persistence of the fever. The patients are urged to drink it *ad libitum*. Moreover, 6-ounce doses of this solution are given every four to six hours during the course of the fever. Apart from small doses of sodium phosphate or potassium sulphate to move the bowels, this was the only medication. Temperatures above 102° F. were treated by sponging with cold water. In conclusion, the author stated that many patients were given acetozone very irregularly on account of several contributory causes: dislike of the taste and odor of the solution; resistance of ignorant patients; lack of assistance on the part of overworked attendants, due to the crowded wards caused by the epidemic. Those patients who are given the drug early, often, and regularly show the best results of this treatment. What Virchow calls the "brutal force of figures" cannot but convince anyone but that acetozone lowers the temperature, shortens the duration of the fever, and lessens its toxic symptoms more than our better known treatments. From the information gained in watching this series of 128 instances of typhoid fever, he believes that where patients can be seen during the first week of the illness and given large amounts of acetozone solution regularly and often, assisted by a gentle laxative, the temperature will return to the normal in from ten to twelve days.—*Therapeutic Gazette*, 1903, No. 3, p. 145.

Disodic-methyl-arsenate.—DR. THOMAS R. FRASER contributes a critical paper on this new, much-lauded cacodylate. In a previous communication he had said that the therapeutic effects of arsenic were caused by its pharmacological action, and if arsenic were united with other bodies so as to be incapable of producing any pharmacological action, or of inducing excessive quantities of toxic effects that represent an extreme degree of pharmacological action, it could no longer be capable of producing the therapeutic effects in the disease which are the recognized effects of arsenic. If, therefore, any compound of arsenic, such as the methyl-arsenates or cacodylates, are found to be so inert that they may be administered without producing—in doses considerably above the minimum lethal of the ordinary active compounds of arsenic—any symptoms of the action of arsenic, it must be because the arsenic ion has been rendered inert, and probably because in

the inert compound the arsenic had formed so firm and stable a union with other ingredients of the compound that no dissociating influence to which it is subjected in the body is able to set free the active arsenic compound or ion from the combination. He showed that in the case of the cacodylates large and even enormous doses may be received by human beings without the manifestation of any toxic symptoms whatever, or of only slight toxic symptoms of arsenical poisoning. It was also shown that in several diseases in which the older arsenical compounds are administered with advantage no therapeutic results assignable to arsenic were obtained; and, further, that when cacodylates are administered they pass through the body and are eliminated in such stable combination with organic bodies that they fail to react to the usual tests for arsenates, and fail to yield arsenium when subjected to the dissociating influence of Marsh's process. Further experience of the cacodylates has also shown that, especially when given in large doses by stomach administration, they frequently cause inconvenient effects, such as a disagreeably alliaceous odor of the breath and skin, gastric disorders, and even congestion of the kidneys, which have been attributed to cacodylic oxide, or binoxide, or to sulpho-cacodylates being generated in certain conditions. These bodies are organic compounds of arsenic and methyl, having a special and distinctive action, which, however, is not the action produced by the ordinary compounds of arsenic and well recognized as that of the arsenic ion in these compounds. To obviate these inconveniences, Gautier has recently introduced another organic compound of arsenic, disodic-methyl-arsenate, $AsCH_3O_3Na_2H_2O$, as a substitute for the cacodylates or di-methyl arsenates. He claims for this salt that while it is non-toxic, it possesses the therapeutic potency of arsenic, and that it has an advantage over cacodylates in so far that it may be used not only by subcutaneous or intramuscular injection, but also by stomach administration, without producing the inconveniences or disorders produced by the generation of minute quantities of cacodyloxide or binoxide. To prevent confusion from the similarity of the chemical names of these two and other methyl compounds, Gautier has introduced the name arrhenal for the disodic-methyl-arsenate. This arrhenal is a colorless, crystalline salt, easily dissolved by water and alcohol, non-hygroscopic, and alkaline in taste and reaction. Silver nitrate causes a white and not a yellow or brick-red precipitate in its solutions, thus failing to produce the reaction of an arsenate or arsenite, although it contains 34.5 per cent. of its weight of arsenium, representing 45.5 per cent. of arsenious acid. It is given in doses varying from 3 grains to 0.38 grain daily. It is claimed to have produced good results in tuberculosis, bronchitis, chorea, syphilis, anæmia and pernicious anæmia, adenitis, leukæmia, influenza, and the vomiting of pregnancy, and it is even stated to have established for itself the position of being the most efficient of all remedies for malaria. The enthusiastic praise of this recently introduced organic preparation of so-called latent arsenic, and the diversity of results in its therapeutic applications, appear to justify an examination similar to that which had previously been made of cacodylates. The general results of the operations that have been brought forward are, that the much-praised disodic-methyl-arsenate, or arrhenal, though containing much arsenic, is practically an inert substance; that, even in enormous quantities, it is incapable of pro-

ducing the well-defined pharmacological action and the well-recognized toxic effects of the arsenic ion; and that, as might in that case confidently be anticipated, it is also incapable of exerting the remedial or therapeutic influences which are those of the older and commonly-used compounds of arsenic.—*The Scottish Medical and Surgical Journal*, 1903, vol. xii. p. 198.

OBSTETRICS.

UNDER THE CHARGE OF

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Bossi's Dilator and Eclampsia.—In the *British Medical Journal*, February 21, 1903, BALLANTYNE reports three cases of eclampsia in which he used Bossi's dilator with great satisfaction.

His first case was that of a primipara, aged twenty-three years, in whom there was posterior rotation of the occiput with a large child. Dilatation was obtained in twenty minutes, followed by craniotomy. The mother made an uninterrupted recovery, and the instrument worked with great satisfaction. His second case was that of a woman in her fourth labor, the os being partly dilated, but labor completely arrested. Dilatation required half an hour in this case, followed by the use of forceps, mother and child making a good recovery. His third patient was a primipara, aged twenty-four years, six and a half months advanced in pregnancy, with very rigid cervix, the os very little open. Dilatation in thirty-five minutes was brought to a little over three inches in diameter. He reports no serious injury following the use of this instrument.

Zangemeister (*Centralblatt für Gynäkologie*, No. 4, 1903) reviews the question of the use of Bossi's dilator in eclampsia, and also the various modifications of this instrument which have been made. He believes that great danger of extensive laceration accompanies the use of this instrument. Personally he has used the original instrument of Bossi, and has taken every precaution to dilate the cervix slowly to avoid laceration. In a fatal case of eclampsia he had the opportunity of examining the uterus, and found two long lacerations of the cervix extending to the peritoneum. He was surprised to find how little force was necessary to turn the dilating mechanism, but he considers this one of the dangerous things about the instrument. He points to the danger of septic infection following laceration of the cervix, in addition to hemorrhage. Personally he much prefers the use of elastic dilators.

Hyperpyrexia with Thrombosis of the Inferior Vena Cava.—FOTHERGILL (*British Medical Journal*, March 7, 1903) reports the case of a patient

delivered by a midwife who had high fever. Retention of the placenta had occurred with infection. A temperature of 111.2° F. was observed, reduced somewhat by hot sponging. Immediately after this thrombosis of the right femoral vein followed, and immediately the same condition in the left femoral vein. There were repeated chills, with great changes in temperature. There was no sign of suppuration or embolus in any other organ. Death ensued from œdema of the lungs. On autopsy the inferior vena cava and its tributaries were filled with ante-mortem clot from the heart downward.

Laceration of the Vagina during Labor.—KAUFMAN contributes to the *Archiv für Gynäkologie*, Band 68, Heft 1, 1903, an extensive paper upon this subject, in which he has collected 82 cases of this complication of labor. But only a portion of these were available for statistical study, as many of them were imperfectly reported.

Most of them occurred when the fœtus presented by the vertex, next in frequency in transverse positions, and least often in breech presentations. In 78 cases, 49 happened in spontaneous labor. In 29, some violent effort at extraction had been made. The condition of the pelvis was reported in 58 of these cases. In 38 the pelvis was said to be normal, and in 20 to have been contracted. In 3 cases myoma of the uterus was present as a complication, and in 1 case a divided uterus, and in 1 scars were found in the vagina and adjacent tissue. Almost all of the patients were multiparæ, as the accident happens very rarely in primiparous patients. In a few of these cases the children were of excessive size, although in most they were of ordinary development. In 68 cases the abdominal cavity was opened through the peritoneal sac. In 14 of these the intestine prolapsed, and in 1 case an ovary and tube. In 29 of these cases the child made its way out of the uterus, in 26 into the abdominal cavity, and in 3 into the subperitoneal tissue.

The placenta was found in 30 cases outside the uterus, in 27 cases in the abdominal cavity, and in 3 cases in the tissue beneath the peritoneum.

As regards the method of delivery most apt to result in injury to the vagina, it was found that version and extraction was especially dangerous, next the forceps, next extraction only, while craniotomy was more apt to produce the accident than eventeration or decapitation. Three of these patients died undelivered.

The treatment of the complication may be divided into those cases in which abdominal section, with or without extirpation of the uterus, was practised, and those cases in which the accident was treated by suture or tampon applied through the vagina. Treatment was selected in accordance with the extent of the laceration and the involvement of the uterus. When the uterus was uninjured and the laceration can be reached from the vulva it was closed by suture; and if the uterus was uninjured and the laceration could not well be reached, tampon and drainage with gauze was the method employed.

The mortality was 35 per cent. in cases where both the uterus and vagina were injured, the most frequent cause of death being septic infection, and next in order hemorrhage.

In cases where the vagina only was injured the mortality was 25 per cent. In these cases the mortality from bleeding was but 5 per cent., septic infection playing the more important part.

The symptoms of this accident depend entirely upon the extent of the laceration. A small rupture of the vagina during labor may give rise to no symptom, and may not be discovered until an examination is made after the birth of the child. Some have laid stress upon the contraction of the round ligaments and upon the suffering and anxiety of the patient. Uterine contractions are not always excessive in these cases, and the patient may not complain of excessive suffering. The mortality from hemorrhage is considerable, and depends upon the extension of the laceration into the connective tissue about the uterus.

In diagnosing the condition, examination by the introduction of the entire hand is necessary to accurately localize the injury.

So far as the prognosis is concerned, the mortality of rupture of the uterus as variously stated at present is from 60 to 73 per cent. The mortality of rupture of the vagina is much less, and may be reckoned at 25 per cent., as has been stated, in favorable and uncomplicated cases.

The prognosis for the children is exceedingly bad in cases of vaginal rupture. The placenta is almost invariably prematurely separated in these cases, and as a consequence the fœtus rapidly perishes. The prognosis for the child is so bad that its interests must not be considered in selecting a method of treatment.

In the treatment of these cases, if laceration happens before the termination of labor, the patient must be delivered as rapidly as possible, no attention being paid to the life of the child; hence, craniotomy or any other method of delivery which will subject the mother to the least violence should be chosen. Perforation of the after-coming head should be employed if the slightest difficulty arises in its delivery. Usually the forceps can be employed to advantage when the head is presenting.

Double Pregnancy in Double Uterus.—In the *British Medical Journal*, March 7, 1903, HELLIER reports the case of a patient, aged thirty-four years, who had had three normal labors previously. During the fourth pregnancy the uterus was larger than usual. After normal labor spontaneous expulsion of a female child occurred by the usual mechanism, its placenta following. It was found that a second child was present, but the physician in attendance, on introducing his hand, found the uterus empty. A second os was discovered high in the pelvis, in front of and to the left of the first. A double uterus was present, and in this second half was a male child, which was delivered by podalic version. The partition between the two halves of the uterus was distinct and quite thick.

Fœtal Ascites.—EDEN reports a case of this comparatively rare condition in the *British Medical Journal*, February 21, 1903. The patient was an unmarried primipara, aged eighteen years, in labor with a footling presentation. The pregnancy was about the end of the eighth month. Labor was very slow; the child died and became macerated. Efforts were made to deliver the fœtus by traction upon the feet. Each traction brought away a

piece of the child until the attending physician could bring away no more. On careful examination it was found that some pathological condition in the abdomen of the fœtus prevented its complete delivery. The abdomen was opened with scissors and several quarts of thin yellowish fluid escaped. The child was then readily delivered. The placenta was adherent, and had to be removed manually. On examining the body of the fœtus the peritoneal cavity was enormously distended, and there were no peritoneal adhesions. The bladder was distended moderately and the urethra was impervious.

GYNECOLOGY.

UNDER THE CHARGE OF

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Progressive Peritonitis.—KREEKE (*Zentralblatt für Gynäkologie*, 1903, No. 7) calls attention to the fact that diffuse septic peritonitis in its early stage is more or less limited, so that, even when the peritoneal cavity seems to be filled with pus, there is a chance of saving the patient by operation, provided that a fatal degree of absorption is not yet present. The limit is thirty-six hours. The writer has had successful cases ranging from five to twenty-eight hours after the onset of peritonitis.

The pulse and temperature cannot be relied upon as positive indications of the severity of the initial infection; nor is tympanites a constant symptom; in fact, the abdomen may be retracted, but extreme tenderness on palpation is seldom absent.

A free median incision should be made, with lateral incisions if necessary. Though irrigation and drainage are all-important, much depends upon the after-treatment of these cases. Nourishment by mouth is avoided until gas passes freely. Enemata of saline solution relieve thirst, and the heart action is stimulated by intravenous infusion, from one to two pints being given every eight hours. Camphorated oil is a valuable stimulant.

Lavage is indicated for the relief of obstinate vomiting. The bowels should be moved early with salines, administered hypodermically if necessary. If intestinal paralysis cannot be overcome, it may be advisable to establish an artificial anus in the ascending colon. In one of the writer's cases the fistula closed spontaneously in six days. With the reappearance of fever new abscesses should be sought for and drained.

In the discussion of this paper before the Munich Gynecological Society, several speakers referred to the value of full doses of atropine in intestinal paralysis.

[The writer has always insisted that in the majority of the successful

cases of cœliotomy for acute septic peritonitis the inflammation was not diffuse, but was limited to the lower half of the abdominal cavity, and was not attended by the systemic infection which is invariably fatal. All cases of more than thirty-six hours' standing are doubtless of this circumscribed character. The writer is able to add a recent successful case in which the operation was performed at the onset of the symptoms, the only indications being, as the writer has stated, general abdominal tenderness and muscular rigidity, without elevation of temperature; in fact, the condition was supposed to be ruptured ectopic.—H. C. C.]

Phenomena following Removal of the Adnexa.—WITSCHEL (*Zentralblatt für Gynäkologie*, 1903, No. 7) tabulates 138 cases from the Strasburg Clinic, in which he notes the fact that there is a marked diminution in the post-operative disturbances following hysterectomy in cases in which the ovaries are preserved. Psychoses were absent. Menstrual molimina were noted more frequently in the latter cases.

Sexual desire persisted in over 50 per cent., whether the ovaries were removed or not, and there was no difference as regarded mental confusion.

Adenoma Malignum in a Young Woman.—URBAN (*Zentralblatt für Gynäkologie*, 1903, No. 7) reports the case of a girl, aged twenty-one years, whose uterus was removed for obstinate hemorrhage. The writer refuses to admit that true adenoma of the uterus is ever a benign neoplasm. He believes that the condition described as adenoma benignum is either glandular polypus or simple glandular endometritis.

Results of Alexander's Operation.—WIELAND (*Zentralblatt für Gynäkologie*, 1903, No. 7) reports thirty-two cases from the Griefswald Clinic, in which subsequent disturbances were noted in only five, such as vesical irritation, dysmenorrhœa, and pain in the cicatrices. Hernia occurred in a single instance; twenty-three patients subsequently became pregnant, eleven being relieved spontaneously, one instrumentally, while seven women aborted. In seven cases (!) the ligaments were torn asunder while making traction upon them.

Venous Stasis as a Cause of Retro-uterine Hæmatocele.—BÜRKLE (*Zentralblatt für Gynäkologie*, 1903, No. 7) believes that hæmatocele is due to general hyperæmia more frequently than is usually supposed, as proved by fourteen autopsies at the Pathological Institute in Prague. He instances the case of a woman, with no history of previous pelvic trouble, who had a severe attack of pneumonia three weeks after her last menstrual period. She suddenly developed tympanites, associated with pain in the lower abdomen, vomiting, diarrhœa, vesical tenesmus, and feeble pulse. A swelling was felt in Douglas' pouch, which was incised per vaginam, and a quart of dark blood was evacuated. The pelvic organs were normal, and careful microscopic examination of the fluid and clotted blood showed no evidence of chorionic structures. The bacteriological examination was negative.

The writer infers that the hemorrhage was a sort of "compensatory or natural venesection."

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Subjective Visual Sensations.—URBANTSCHITSCH (*Klin. Therap. Wochen.*, 1902, No. 45) made a series of experiments upon a large number of healthy persons, hysterical and neurasthenic subjects excluded, upon subjective influence on visual sensations. After prolonged fixation of a quiescent, narrow object (a window-sash or a line) the same appears to many persons to become crooked, to waver, or to oscillate. Cross-lines also appear to revolve about their point of intersection (deceptive movements). Individuals inclined to vertigo are especially apt to observe this phenomena in marked degrees. Fixed points also show similar movements—jumping, waving, swaying, oscillating, or revolving Such movements had already been noticed by Humboldt to affect the stars (stellar swayings). Exner explained this as being due to inexact localization of visual impressions. The occurrence of such deceptive movements is furthered by various stimuli (tactile, thermic, electric, acoustic), whereby a different movement—but as it seems constant for the same individual and the same stimulus—corresponds to different stimuli. Such movement, however, is not the same, even to the same stimulus for both eyes. It may thus happen that the movement ceases during binocular vision, and the point is quiescent; whereas, in monocular vision the movements seem to take place in opposite directions for each eye separately, cancelling one another during binocular vision. The movements are called forth even by weak galvanic currents.

While observing a black point many persons notice beside it a false image in the form of a dark disk, a semicircle, a square, etc. This image is normally quiescent. Upon application of the above-mentioned stimuli it is seen to move, changed in form, or perhaps observed only then, and that, too, in a manner characteristic of the particular stimulus, or even of the particular portion of the body which has been stimulated. Such appearances also arise while observing a white surface, if a stimulus is allowed to act upon the observer. Appearance and kind of stimulus stand, as it seems, in the same individual in a constant relation to one another. These appearances are not called forth, modified, or set in motion by actual tones, but rather through an acoustic after-sensation. They may be different upon stimulation of the left auditory apparatus from that of the right.

These subjective movements may be further modified by looking at the object through a colored glass. Upon observing colored lines coincidently with certain stimuli—*e. g.*, a tone—subjective images of characteristically colored lines appear; for example, with deep notes the images are red; with

high notes, green. The form of these subjective images also depends upon the color of the surface upon which they appear. Such an image, if it be looked at through two differently colored glasses (*e. g.*, red before one eye, green before the other), becomes decidedly changed in color through some stimulus, *e. g.*, a tone, passing from red to green, showing a mixture of colors or colored spots. If three differently colored adjacent fields are looked at and a stimulus is made to affect the body, a particular one of the fields, according to the nature of the stimulus—*e. g.*, the pitch of the tone—enlarges, contracts, or even disappears. The color of optical after-images is also changed by various stimuli. In this way a positive after-image may be changed into a negative one; so, likewise, after-images looked at at the same time through two differently colored glasses are changed by stimuli (auditory, gustatory, tactile, etc.); in color they appear mixed or parti-colored. It is an interesting fact that acoustic after-images are able to modify optical images in an analogous manner. When a colored surface is looked at subjective images—*e. g.*, spots, geometrical figures, etc.—appear thereon, determined by various stimuli. It is a strange fact that they may be excited even by the remembrance of a tone. They then correspond to the after-image which arises when the tone is actually heard. A white surface changes, if a colored one is strongly called up in imagination, into that color, and after-images also appear. An after-image already present may be changed in color if that color is called up in imagination. If, while regarding a subjective colored surface another color is thought of, the surface goes over first into a mixture of the two colors, and finally into that of the second. It is possible in this way to mingle objective colors with subjective. An actual red surface appears violet if blue be called up in imagination.

The Cosmetic Value of Paraffin Injections after Enucleation of the Eyeball.—RAMSAY, Glasgow (*Lancet*, January 31, 1903), records his experience in the use of paraffin in 22 cases for forming a stump on which to fit an artificial eye. His method of procedure is as follows: The conjunctiva is divided as close as possible to the corneal margin. Each rectus muscle is caught up on a strabismus hook and sutured to the overlying conjunctiva with a strand of catgut. The tendons of the recti muscles are cut at their insertion into the sclerotic, and thereafter the operation for the removal of the eyeball is completed in the ordinary manner. The capsule of Tenon is packed with gauze till a strong black silk purse suture has been passed around the conjunctival margin, and then, the packing being removed, the melted paraffin is injected with a carefully sterilized glass syringe, the capsule being opened to its utmost capacity by holding the recti muscles on the stretch by means of the four catgut sutures and filled to overflowing. The purse suture is then tightened and securely fixed by a double knot, and the catgut sutures are tied, the superior rectus muscle being approximated to the inferior and the internal to the external.

This operation is followed by very little inflammatory reaction. The purse suture is removed in two weeks, at which time there will be found over the freely-movable paraffin stump a clean, non-discharging surface of conjunctiva. A week later an artificial eye can be adjusted.

To ensure success two points require special attention. First, the operation must be carried out with every precaution against sepsis, and so it must not be attempted in cases where the eyeball is in a state of active suppuration; and, secondly, the sutures must hold the conjunctiva in accurate position over the paraffin. It is important to see that an equal grip is taken of the conjunctiva all around the free edge, and that too wide an interval is not left between the stitches.

There were four failures in Ramsay's 22 cases. In one case after the enucleation of a supporting eyeball pus appeared in the socket and set up so much inflammatory reaction that the stitches were removed and the moulded paraffin allowed to escape. In 3 cases the paraffin came out through inefficiency of the stitching. The 18 remaining cases gave a satisfactory cosmetic result, with free movement of the prothesis.

PATHOLOGY AND BACTERIOLOGY.

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Symposium on Snake Venom: 1. The Poison of Serpents, MITCHELL. 2. Venom and Antivenene, MCFARLAND. 3. A Comparative Study of Snake Venom and Snake Sera, NOGUCHI (*Proceedings of the Pathological Society of Philadelphia*, February, 1903, vol. vi., No. 4).—Mitchell opened this symposium with an interesting historical introduction. Bonaparte had indicated the albuminous character of snake poison in 1843. Mitchell began his researches on snake venom in 1857, and at intervals continued them until 1899, both alone and in connection with Reichert and Stewart. The general toxicity, pathology, and action of venom on the blood were so completely worked out as to leave only a few points undetermined. During the last two years Flexner and Noguchi have worked on snake poison in the light of the recent important theories of immunity inaugurated by Bordet and Ehrlich.

Calmette has succeeded in immunizing horses against cobra poison by heating the venom to 70°, which removed the local irritating poison while not affecting the neurotoxin. McFarland began immunizations with cobra venom on Calmette's principle. On turning his attention to immunization against rattlesnake venom, an extremely irritative local poison made the injection of large animals wellnigh impossible. At the end of a year, however, the horse serum possessed protective powers against the neurotoxic

principle of both cobra and rattlesnake venom and gave precipitates with rattlesnake venom markedly, and with cobra venom to a less extent.

The work of Flexner and Noguchi has been important as confirmatory of Ehrlich's lateral chain theory of immunity. It was found that the various venoms act as an intermediary body to bring about hæmolysis of the blood of susceptible animals in presence of the blood serum, which completes the hæmolysis by its complementing action. In most cases, in the absence of serum, no hæmolysis takes place. Whenever it does, however, the lysis of the corpuscles has been shown by Kyes to be due to an endocomplement within the blood cells. Unmodified snake serum also produces hæmolysis, but when heated to destroy the complement is not hæmolytic, and does not recover complement from the serum of the alien blood, in this respect differing in its action from venom. Venom itself when fresh contains no complement, but is reactivated by snake complement as well as by the complement of susceptible bloods. The serum of animals inoculated with heated rattlesnake serum protects against the hæmolytic action of rattlesnake serum, and the venoms of rattlesnake, cobra, and moccasin.

The Pancreas in Cirrhosis of the Liver.—STEINHAUS (*Deut. Arch. f. klin. Med.*, 1902, Bd. 74, p. 587) made a study of the pancreas in twelve cases of cirrhosis of the liver. In all, except one instance, the pancreas showed a more or less grave chronic inflammation. The one exception was a typical case of Laennec's cirrhosis of the liver. The chronic inflammatory changes in the pancreas consisted in a connective tissue growth, which was sometimes of a perilobular type, sometimes of a periacinar type, and although occasionally the parenchyma of the organ was in large part replaced by fibrous tissue, in no case were the islands of Langerhans involved. These structures appeared to be normal in every case. A transient glycosuria was noted in one case, and the author calls attention to the possible relation which may exist between chronic inflammatory lesions of the pancreas and the alimentary glycosuria of cirrhosis of the liver.

Ring Bodies (Nuclear Remnants) in Anæmic Blood.—CABOT (*Journal of Medical Research*, 1903, vol. ix. p. 15), using Wright's modification of Leishmann's stain in studying the blood from cases of anæmia, observed peculiar stained ring formations within certain of the red blood corpuscles. These figures were seen in three cases of pernicious anæmia, four of lead poisoning, and one of lymphatic leukæmia. Unlike the ordinary basophilic granulations found so often in the red blood cells from cases of lead poisoning and pernicious anæmia, these figures stained not blue, but bright red. The rings were quite perfect. They varied in size: in some instances being very small, in others encircling the extreme periphery of the corpuscle. Rarely they were twisted or had a figure-of-eight form. Occasionally basophilic granulations were noted in the same corpuscle which contained a ring body. Such figures did not appear in blood specimens stained with hæmatoxylin. The author believes that they may be connected in some manner with cell regeneration, and suggests that they may represent nuclear remains, or, perhaps, portions of the nucleus which have resisted those forces destructive to it, and ultimately to the cell itself.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Action of Water on Lead.—Dr. S. Ruzicka (*Archiv für Hygiene*, xli., p. 23) has conducted a series of experiments with distilled water and with solutions of salts of calcium, magnesium, potassium, sodium, and ammonium (sulphates, chlorides, carbonates, and nitrates) on clean lead pipe under various conditions, as contact with air, exclusion of air, renewal of the solutions, mixing of solutions, etc., and has determined the amounts of lead taken up in each case. Water containing carbon dioxide, and solutions containing organic matter from grass, peat, radish leaves, and fish flesh were tried, also. He concludes as follows: 1. The influence of inorganic salts in solution is independent of the nature of the base, but is due wholly to the combined acids. Nitrates in solution cause almost as much corrosion as does distilled water, but chlorides, sulphates, and carbonates exert a restraining action, the intensity of such influence being greatest with the last mentioned. 2. With combined solutions of salts the order of the restraining influence of the several salts is, from least to greatest, nitrates, chlorides, sulphates, carbonates. Carbonates always diminish the rate of corrosion by the other three; sulphates, that by chlorides and nitrates; chlorides, that by sulphates and nitrates; and nitrates always increase the action of the other three. 3. If lead comes continuously in contact with fresh portions of a carbonate solution, the amount of lead given up, small in any event, diminishes progressively. 4. A relatively small amount of carbonate can overcome the influence of nitrate (6 carbonate to 10 nitrate), but when it falls at all below the necessary amount (to 5 parts, for instance), the action increases at once. 5. Free carbon dioxide, contrary to general belief, causes diminished action with both distilled water and the salt solutions. 6. The organic matters of peat increase corrosion; those of the other substances employed inhibit it. 7. Carbonates, carbon dioxide, and extracts of grass and of radish leaves exert greater inhibitive influence than the other substances used. Under all conditions, access of air results in increased corrosion.

The restraining influence of carbon dioxide is testified to also by F. Clowes (*Proceedings of the Chemical Society*, 1902, vol. xviii. p. 46), whose experiments yielded results substantially, but not wholly, in agreement with the above. He found that soluble sulphates and sulphuric acid exert a greater restraining influence than that of the carbonates. Calcium hydroxide in large amounts promotes corrosion. He determined the nature of the compound of lead resulting when pure lead is brought into contact with ordinary distilled water. Considerable lead goes into solution, probably as hydroxide; but, on filtering, a lead compound soluble in cold acetic acid remains on the paper. This

was found to be a hydroxy-carbonate containing three molecules of carbonate and one of hydroxide ($3PbCO_3.PbO_2H_2$). The first reaction with aërated water appears to be oxidation and formation of hydroxide, which then is precipitated by carbon dioxide as basic carbonate.

Disinfection by Dry Heat.—SCHUMBURG (*Zeitschrift für Hygiene und Infectionskrankheiten*, xli. p. 167) shows that, although dry hot air is so uncertain in its action as to be unsuitable for practical disinfection, air at 100° C. will kill the most resistant non-sporing bacteria in and on clothing and other objects within an hour, if it contains from 55 to 65 per cent. relative humidity. This degree of moisture can be attained by having a vessel of water in the space where the objects are treated. Since disinfection of clothing and other objects containing anthrax and tetanus spores is very seldom needed, and since, on the other hand, the bacteria most commonly the object of disinfection (those of typhoid fever, cholera, plague, influenza, diphtheria, tuberculosis, and, probably, measles and scarlet fever, and the pus cocci) form no spores, disinfection with moist hot air will suffice in almost all cases. This method has this advantage over disinfection by steam: that articles of leather (gloves, books, riding breeches, etc.) may be exposed from six to eight hours without injury.

The Neutral-red Method in the Differentiation of B. Coli and B. Typhosus.—A systematic test of a number of races of coli and typhoid organisms with neutral-red has been made by M. P. FITZGERALD and GEORGE DREYER (*Biochemisches Centralblatt*, March 1, 1903, p. 238), who used peptone bouillon and agar containing 0.5 or 1.0 per cent. aqueous solution of neutral-red and varying amounts of acid, alkali, and glucose. They found but one qualitative difference between *B. coli* and *B. typhosus*, and hence, one cannot be satisfied with this one test alone. Glucose-free bouillon is preferable to agar. Large amounts of acid interfere with the reaction, and one must avoid the presence of 0.5 per cent. or more of glucose. The best medium appeared to be 3 per cent. lactose bouillon with the above-mentioned amount of neutral-red. In four to six days, *B. typhosus* gives a yellow color, while *B. coli* gives a red. The original color of the liquid has no influence on the end result. When the typical color once appears it persists. The result is less dependent upon the amount of free acid or alkali than with other methods. Different samples of neutral-red appeared to be reducible in different degrees.

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INDEX.

ABDOMINAL pain, case of obscure, 538
Ablation of the crystalline lens to rectify high myopia, 551
Abscess of liver, 210
of uterus, 171
Abscesses of the liver following typhoid fever, 618
Actinomyces-like development of some of the acid-resisting bacilli, 373
Actinomycosis of the occiput, 179
Action of water on lead, 1117
Acute articular rheumatism, relapses of, 343
Adenoma malignum, 738, 1112
of nose, 176
Adnexa, removal of, 1112
Adrenal tumors, 33
Adrenalin glycosuria, 46
toxicology of, 727
Affinity of carbonic oxide for hæmoglobin, 167
Agglutination in mixed infections and their means of diagnosis, 937
Agurin, a new diuretic, 351
Air, entrance of, into veins, 519
passages, foreign bodies in, 743
Alcohol as a disinfectant, 739
Aldrich, C. J., aphasia in acute disease, 431
Alexander's operation, results of, 1112
Alkaline Vichy waters, 932
Alkaptonuria, incidence of, 531
Allen, H. W., paracolon infections, 96
Alopecia areata of the moustache, 932
Amyotrophic lateral sclerosis, 939
Anæmia, report of cases of, 397
Anæsthesia, 729
Anastomosis of the portal vein with the vena cava, 535
Anatomy and surgery of temporal bone, 543
of chronic parametritis, 550
Anders, J. M., jaundice, 596
Aneurism of transverse portion of aortic arch, 778
operation for radical cure of, 723
Angiofibroma of nose, 742
Angiomata, 534
Antagonism of morphine and cocaine and the employment of cocaine in morphine poisoning, 164
Aortic arch, aneurism of, 778
Aphasia in acute disease, 431
Appendicitis, acute, 1102
recurrent, 725
Arsenic in phthisis, 166
in Sydenham's chorea, 729
Articular rheumatism and some allied conditions, 412
Artificial distention of bladder, 171
sterilization, 362
Atrophy of eyeball, 368
of uterine mucosa, 924

BACILLUS of Eberth, presence of, in blood of typhoid fever patients, 938
of typhoid fever, viability of, 913
Bacteria, growth of, in the intestine, 535
in oils, presence and vitality of, 186
Bacteriological findings in an epidemic of dysentery in Southern Syria, 374
Bacteriology of empyema in children, 732
of otitis of measles, 929
Bacteriolytic power of blood, changes in, after typhoid vaccination, 935
Banti's disease, case of, 405
Bence Jones albumosuria, 658
Benign epithelial proliferation in the corpus uteri, 738
Beriberi, causation of, 184, 588
Bladder, artificial distention of, 171
Blood pressure determinations, clinical value of, as a guide to stimulation in sick children, 433
reaction of acute cerebral compression, 1017
Bossi's dilator and eclampsia, 1108
in rapid dilatation of uterus, 358
Boston, L. N., Bence Jones albumosuria, 658
Brain of the horse, some principles of, 354
Briggs, C. E., intestinal perforation during the course of typhoid fever, 821
Brown, L., zomotherapy in tuberculosis, 1071
Bullæ in lichen planus, occurrence of, 178

CÆSAREAN section by transverse incision of fundus, 736
for placenta prævia, 548
Camphor and morphine disease, 165
Cancer of Fallopian tube, 925
of uterus, radical operation for, 740
treatment of, 362
Cancerous affections of skin, treatment by means of the X-rays, 539
Carcinoma of stomach, presence of elastic tissue in, 557
X-ray treatment of, 352
Cataract, incipient, treatment of, 183
Chadbourne, T. L., upon the association of epilepsy and heart disease, 461
Chemical individuality, a study in, 531
pathology of the saliva and of the pharyngeal secretions as a means of diagnosis, 178
Chloride of ethyl in anæsthesia, 726
Cholecystitis, gangrenous, 592
Chondrodystrophia fœtalis, 751
Choroid, metastatic carcinoma of, 375
Chyluria, non-topical, 721
Circulatory disturbances in collapse in acute infectious diseases, 720
Cirrhosis of liver, 215
Clarke, M. A., memoir of J. M. Da Costa, 318
Club-foot, paralytic, 162
Cohen, S. S., tropical abscess of liver, 210
Coins in œsophagus of infants, 927
Collins, J., amyotrophic lateral sclerosis, 939
Congenital dislocation of the shoulder, 967
Cook, H. W., the clinical value of blood pressure determinations as a guide to stimulation in sick children, 433
Cortical centres of vision as demonstrated after enucleation or atrophy of the eyeball, 368
Craig, C. F., Malta fever, its occurrence in the United States Army, 105
Cumston, C. G., congenital dislocation of the shoulder, 967
Cushing, H., blood-pressure reaction of acute cerebral compression, 1017
Cyst of pancreas, 553
Cysts, ovarian, 6

DA COSTA, J. M., memoir of, 318
Deaver, J. B., diseases of pancreas, 187
Decomposition of iodides in the body, 354
Dermatitis coccidioides, 931
occurring during typhoid fever, 181
verrucosa probably caused by the bacilli coli communis, 179
Dermatoses occurring in exophthalmic goitre, 1000
Dermoid cysts, 6
Diabetes in gynecological operations, 551
insipidus, 532
Dillard, H. K., epicarin in tinea tonsurans and tinea circinata, 1012
Diphtheria bacilli, report on, 372
serum question, 166
Diphtheritic conjunctivitis, 183
Disinfection by dry heat, 1118
of hands by hot water and alcohol, efficiency of, 735
Disodic methyl-arsenate, 1106
Double pregnancy in double uterus, 1110
Drinking water, distribution of sewage bacteria in, 560
Droplets and dust, infection through, 561
Drops as dose measures, 352
Duodenal region, peritonitis of, 882
Dupuytren, fracture of, 349
Duration of lactation, 546
Durham tube in right bronchus, 177
Dwarf, short-limbed, anatomical study of, 751
Dyspepsia, relation of, to pelvic disease, 923

ECLAMPSIA, production of, 547
Edsall, D. L., nature and treatment of recurrent vomiting in children, 629
Elastic bags, vaginal use of, 174
Ellis, A. G., the pathology of the tissue changes induced by the X-ray, 85
Empyema, bacteriology of, 732
Entrance of air into the veins, 519
Eosinophilia in pelvic lesions and in the vermiform appendix, 74
Epicarin in tinea tonsurans and tinea circinata, 1012
Epiglottis, lupus of, 928
Epilepsy and heart disease, 461
Ergot, preparation of, 736
Erythema scarlatiniforme desquamativum recidivans, 934
Erythematous keratodermia, 933
Eshner, A. A., unilateral renal hæmaturia, 636
Estimation of the transverse diameter of the pelvis in the parturient woman, 175
Ethyl chloride in treatment of incurable cancer, 365
Experimental investigations upon the new formation of inflammatory granulation tissue, 554

External dorsal luxation of the metacarpophalangeal joint of the thumb, 347
Extogan, 918
Extremities, fractures of, treatment of, 540
Eye, wounds of, treatment of, 367
Eyeball, atrophy of, 368

FACE presentation, operative treatment of, with posterior turning of chin, 360
Fake morphine cure, 165
Fallopian tube, cancer of, 925
Falsetto voice, 928
Fat absorption, question of, in the intestinal canal and the transport of fat to other organs, 556
Favus of scrotum, 931
Femoral hernia, Roux's operation for, 727
osteotomy and ostectomy in ankylosis of the hip in malposition, 348
Fever of infancy, 745
Malta, 105
Fibres, course of, in the optic nerve, 366
Fibromyoma complicated with pregnancy, 548
of urethra, 171
Fibrosarcoma of tonsil, 176
Fiebre de Barras, 745
Field, C. W., case of Banti's disease with diffuse productive nephritis, 405
Findley, P., hydatiform mole, 486
Flexion deformity at knee-joint, new method of correcting, 770
Fœtal and maternal blood serum, 920
ascites, 1110
Folliculoma, malignant, of ovary, 363
Foot, pronation of, 775
Fracture of Dupuytren, 349
Fractures of extremities, treatment of, 540
Freezing, effects of, and other low temperatures upon the viability of the bacillus of typhoid fever, 913

GALLSTONE disease, 851
Gangrene of lung, case of, 1060
Gangrenous cholecystitis, 592
Garceau, E., ureteritis in the female, 284
Gastric ulcer, perforating, 1101, 1102
Gelatin injections, dangers of subcutaneous, 352
Genital tuberculosis, diagnosis of, 550
Gestation, tubal, 545
Gibbon, J. H., gangrenous cholecystitis, 592
tropical abscess of liver, 210
Glanders, disease clinically resembling, in Philippine Islands, 935
Gonococcus in pregnancy and the puerperium, influence of, 362
Gonorrhœa, argyrol in, 163
Gonorrhœal endocarditis, with cultivation of the specific organism from the blood during life, 555
vulvovaginitis in children, 311
Good, C. A., an experimental study of lithium, 273
Goodridge, M., entrance of air into the veins, 519
Gould, A. H., complete bilateral duplication of the ureters, 428
Graves' disease, treatment of, 542
Guaiacol valerianate in phthisis, 730

HÆMATURIA, unilateral renal, 636
Hæmolytic complement, study of, found in the serum of the rabbit, 936
Hall, J. N., late systolic mitral murmurs, 663
Hamill, S. McC., review of some of the older writings on infant feeding, 1044
Heart, working capacity of, 911
Hektoen, L., anatomical study of a short-limbed dwarf, with special reference to osteogenesis imperfecta and chondrodystrophia fœtalis, 751
Hemmeter, J. C., concerning the rôle of intracellular catalytic processes in the pathogenesis of malignant neoplasms, 666
Hemorrhage from a ruptured ovisac, 923
Hernia, 799
Heroin and dionin, action of, on respiration, 541
Herpes of larynx during menstruation, 363
zoster, 256
Herter, C. A., on adrenalin glycosuria and certain relations between the adrenal glands and carbohydrate metabolism, 46
Hodgkin's disease, pathological changes in, 370
Hopogan, 918
Hospital notes, 1079
Hot air in gynecological treatment, 548
House epidemic of a fever simulating typhoid caused by an atypical colon bacillus and traced to the water supply, 556
Howard, W. T., pathology of labial and nasal herpes and of herpes of the body occurring in acute croupous pneumonia and their relation to the so-called herpes zoster, 256

Hubner, E. J., pronation of foot, 775
Human and bovine tuberculosis, relationship between, 937
blood pressure, study of, in some pathological conditions, 888
Hydatid costal cysts, 1103
Hydatiform mole, 486, 737, 920
Hyde, J. N., dermatoses occurring in exophthalmic goitre, 1000
Hyoscine for morphine disease, 919
Hyperpyrexia with thrombosis of inferior vena cava, 1108
Hyphomycetic granuloma of the skin, 178
Hypodermic purgatives, 543

ICE as a vehicle of infectious disease, 913
Impermeability of the lung for ammonia, 167
Infant feeding, 1044
Infantile scorbutus and sterilized milk, 733
Infection through droplets and dust, 561
Infectious paracolon, 96
Inheritance and intra-uterine transmission of the agglutinating properties of the blood and the formation of agglutinins in the bodies of embryos, 745
Injections of yolk of egg for tuberculosis, 541
Intestinal perforation during the course of typhoid fever, 821
Intestine, growth of bacteria in, 535
volvulus of small, 799
Intra-abdominal pressure, 169
Intracapsular prostatic resection, 507
Intracellular catalytic processes, rôle of, in the pathogenesis of malignant neoplasms, 666
Intraperitoneal hemorrhage and ectopic gestation, 921
Intravascular antisepsis, 1105
Inversion of uterus, complete, 360
Iodides, decomposition of, in the body, 354

JAUNDICE, a contribution to the toxic forms of, 596
Jelke, W. F., studies of ovarian embryomata or so-called ovarian dermoid cysts, 6
Jelliffe, S. E., notes on the opium habit and its treatment, 786

KELLY, A. O. J., multiple serositis, 116
Knee-joint, new method of correcting flexion deformity, 770
Krauss, W. C., sarcoma of the third cervical segment, 1

LABIAL and nasal herpes, pathology of, 256
Laceration of vagina during labor, 1109
Lacrymal gland, nerve supply of, 182
Lactation, duration, 546
Laparotomy during pregnancy, 549
for adherent retroflexion during pregnancy, 168
Larynx, foreign body in, 742
herpes of, during menstruation, 363
morbid growth of, 742
Le Boutillier, T., aneurism of transverse portion of aortic arch, 778
Leucocytic count in the diagnosis of diseases of children, 355
Leucocytosis in pelvic suppuration, 739
Ligation of internal iliac and ovarian arteries in cancer of uterus, 365
Lithium, an experimental study of, 273
Liver, cirrhosis of, 215
tropical abscess of, 210
Loeb, L., mixed tumors of the thyroid gland, 243
Lupus erythematosus, treatment of, 932
of epiglottis, 928
vulgaris, treatment of, 180
Lymphangiectasis of vulva, 168
Lymphosarcoma of uterus, 923
Lymphotoxic and myelotoxic intoxication, pathology of, 373

McEWEN, E. L., dermatoses occurring in exophthalmic goitre, 1000
Malaria, methylene blue and quinine in, 916
Malarial fever in Texas, 448
treatment of, 345
Malignancy of solid embryomata, 170
Malignant neoplasms, pathogenesis of, 666
Malta fever in the United States Army, 165
Mannitol pentanitrate, 542
Marsh, J. P., multiple melanotic sarcoma unsuccessfully treated by X-rays, 238
Maxillary sinus, sarcoma of, 928
Membranous glossitis, fatal, 177
Memoir of J. M. Da Costa, 318
Menopause, 171
premature, 168
Mesentery, torsion of entire, 799
Metabolism in albuminuria, 1099
Metacarpophalangeal joint of thumb, external dorsal luxation of, 347
Micrococcus of acute rheumatism, 1100
Mitral murmurs, late systolic, 663
Mole, hydatiform, 486, 737, 920

Morphine addiction and its treatment, 917
disease, hyoscine for, 919
physiological action of, 353
poisoning, 164
Multiple melanotic sarcoma unsuccessfully treated by the X-rays, 238
progressive hyaloserositis, 743
sclerosis, cases of, 61
serositis, 116
Mycosis fungoids and its treatment by the X-rays, 933
Myelogenous leukæmia, 984
Myomectomy and castration, results of, 922
Myopia, etiology of, 181, 366

NASAL diphtheria, primary, 926
polypi the cause of atrophy of the optic nerves, 742
Nephritis, acute, following mumps, 911
Neuroses and mastoid operations, 930
Neutral-red method in the differentiation of B. coli and B. typhosus, 1118
Noma and hospital gangrene, 180
Non-tropical chyluria, 721
Norris, G. W., study of the human blood pressure in some pathological conditions, 888
Nose, adenoma of, 176
angiofibroma of, 742
morbid growths of, 741
saddle-back, 926

OATMAN, E. L., metastatic carcinoma of the choroid, 375
Œdema, persistent, 157
Œdematous laryngitis, 176
Œsophagus of infants, foreign bodies in, 927
Operative procedure, a new, 535
Ophthalmia neonatorum, treatment of, 368
Opium habit and its treatment, 786
Optic neuritis in diphtheria, 551
Osteogenesis imperfecta, 751
Osteosarcoma of inferior turbinate, 741
Otitis of measles, bacteriology of, 929
Ovarian embryomata, studies of, 6
parotitis, 740
tumors complicating pregnancy, 365
Ovary, malignant folliculoma of, 363

PANCREAS, cyst of, 553
diseases of, 187
in cirrhosis of liver, 1116
Papilloma of nasal septum, 741
Paracolon infections, 96
Paraffin injections, cosmetic value of, after enucleation of the eyeball, 1114
Paralytic club-foot, operation for, 162
Parametric cicatrices, treatment of, 922
Parametritis, chronic, anatomy of, 550
Paratyphoid fever, an epidemic of, 719
Paravaginal incision in hysterectomy, 169
Park, R., sarcoma of the third cervical segment, 1
Parotiditis, 926
Parotitis after ovariotomy, 364
Pathogenesis of malignant neoplasms, 666
Pathology of the tissue changes induced by the X-ray, 85
Pelvic suppuration, treatment of, 550
Pennyroyal, poisoning from, 166
Perforation of uterus, 169
Peritonitis, progressive, 1111
Peridynamin, 351
Peritonitis of duodenal region, 882
Persistent hereditary œdema of the lower limbs, 157
Pfahler, G. E., case of gangrene of lung, 1060
Phenolphthalein as a purgative, 543
Philippine Islands, disease resembling glanders in, 935
Phlegmonous laryngitis, 177
Phlyctenular keratitis, treatment of, 552
Phthisis, arsenic in, 166
guaiacol valerianate in, 730
Physical therapy, 352
Piles, simple method of operating on, 1104
Pneumonia, treatment of, 540
Polymyositis, acute, 158
Pregnancy and labor complicated by atresia and stenosis of vagina, 735
Pronation of foot, 775
Prostatic hypertrophy, 537
Pruritus vulvæ, 924
Pseudaconitine and japaconitine, 542
Psoriasis following nervous shock, 179
vaccination, 180
Ptomaine poisoning, 747, 749
Pubiotomy, 172
Pulmonary embolism following hysterectomy, 364
phthisis, new system of treating, 916
Purgatives, hypodermic, 543
Putnam, J. W., sarcoma of the third cervical segment, 1

QUININE in malaria, 916
Quintuplets, 175

RAYNAUD'S disease, vasomotor spasm of, 346
Recurrent vomiting in children, 629
Relations between the lymphatics and the connective tissue, 746
Resection of nearly eight feet of gangrenous intestine, 161
Restoration of sight in a nearly blind cancerous eye by cancroin, 553
Retroflexion, treatment of, 551
Retroperitoneal lipoma and uterine fibroid, 365
Retro-uterine hæmatocele, 1112
Reviews—
American Edition of Nothnagel's Encyclopædia, 149, 153
Ballance, The Healing of Nerves, 337
Brownell, Anatomy and Histology of the Mouth and Teeth, 907
Brubaker, Human Physiology, 904
Buck, Reference Handbook of the Medical Sciences, 530
Buller, Text-book of Materia Medica, Therapeutics, and Pharmacology, 716
Cattell, International Clinics, 341
Charaka-Samhita, 340
Chase, General Paresis, Practical and Clinical, 708
Cheyne, Manual of Surgical Treatment, 332
Cohen, A System of Physiologic Therapeutics, 339
Crile, Experimental and Clinical Research into Certain Problems Relating to Surgical Operations, 338
Crothers, Morphinism and Narcomania, from Opium, etc., 336
Cryer, Internal Anatomy of Face, 711
Culbreth, Manual of Materia Medica and Pharmacology, 906
Defendorf, Clinical Psychiatry, 712
Doflein, Die Protozoen als Parasiten und Krankheitserregen, 908
Dudley, Principles and Practice of Gynecology, 150
Eckley, Manual of Dissection for Practical Anatomy, 910
Ekgren, Pocketbook on Massage, 335
Eyre, Bacteriological Technique, 1097
Fox, Treatise on Smallpox, 337
Gerrish, Text-book of Anatomy, 718
Gould, American Year Book of Medicine and Surgery for 1903, 713
Graham, Treatise on Massa e 335
Reviews—
Grant, Surgical Diseases of the Face, Mouth, and Jaws, 904
Grayson, Diseases of the Throat and Nose, 334
Grünwald, Atlas of Diseases of the Mouth, Pharynx, and Nose, 907
Hare and Landis, Progressive Medicine, 713, 908
Hare, Text-book of Practical Diagnosis, 340
Hartmann, Chirurgie Gastro-intestinale, 340
Head, The Practical Medicine Series of Year Books, 530, 909
Hemmeter, Diseases of Stomach, 709
Herter, Chemical Pathology in Its Relation to Practical Medicine, 715
Hutchison and Rainy, Clinical Methods, 714
Kayser, Diagnosis and Treatment of Nose, Throat, and Ear, 1098
Kirmisson, Les Difformités Acquises de l'Appareil Locomoteur Pendant l'Enfance et de l'Adolescence, 715
Kolle and Wassermann, Handbook of Pathogenic Microörganisms, 706
Koplik, Diseases of Infancy and Childhood, 528
Le Fevre, Physical Diagnosis, 717
Leroy, Essentials of Histology, 717
Mattison, Morphinism, 1098
Medical News Visiting List for 1903, 156
Mell, Biological Laboratory Methods, 529
Oertel, Medical Microscopy, 712
Physician's Visiting List for 1903, 156
Politzer, Diseases of the Ear, 155
Posey and Wright, Diseases of the Eye, Ear, Nose, and Throat, 524
Potter, Handbook of Materia Medica, Pharmacy, and Therapeutics, 527
Report on the Collective Investigation Made by the Committee for the Investigation of Cancer, 152
Reynolds and Newell, A Manual of Obstetrics, 155
Schleif, Materia Medica, Therapeutics, Medical Pharmacy, Prescription-writing, and Medical Latin, 903
Schmaus, Text-book of Pathology and Pathological Anatomy, 905
Schmidt, Manual of Genito-urinary and Venereal Diseases, 712

Reviews—
de Schweinitz, Diseases of the Eye, 525
Sen, Treatment of Tropical Diseases 342
Soupault, Dilatation of Stomach, 527
Stelwagon, Diseases of the Skin, 330
The Public and the Doctor, 530
Thresh, Water and Water Supplies, 342
Traité de Chirurgie Clinique et Operatoire, 341
Tyson, Examination of Urine, 1097
Van Schaick, Regional Minor Surgery, 909
Warren and Gould, International Textbook of Surgery, 707
Woolsey, Applied Surgical Anatomy, 1095
Yeo, Manual of Medical Treatment on Clinical Therapeutics, 905
Rheumatism, acute articular, relapses of, 343, 412
Rhubarb, active principles of, 730
Riesman, D., case of gangrene of lung, 1060
Ring bodies in anæmic blood, 1116
Ringworm of thigh, 931
Robinson, B., study of some cirrhoses of the liver, 215
Roux's operation, value of, for the radical cure of femoral hernia, 727
Rubber tissue as a dressing, 704
Rubella scarlatinosa, 731

SADDLE-BACK nose, 926
Sarcoma of branchial cleft, 741
of maxillary sinus, 928
of third cervical segment, 1
Scarlatiniform erythema in tuberculosis, 533
Schmitt, A. E., anatomy and surgery of the temporal bone, 563
Sclerosis, multiple, cases of, 61
Scorbutus, infantile, 733
Scott, J. A., report of cases of anæmia, 397
Scurvy, 749
Senile cataract, when to operate for, 552
Sense of sight, study of, 182
Sensibilizers of sera active against albuminoid substances, 373
Serositis, multiple, 116
Serum of Trunecek in arterio-sclerosis, 351
Serumtherapy of typhoid fever, 936
Sewage bacteria in drinking water, 560
Sheldon, J. G., abscesses of the liver following typhoid fever, 618
Simon, C. E., myelogenous leukæmia, 984
Smith, G. T., rubber tissue dressing, 704
Snake venom, symposium of, 1115
Sodium and potassium iodides and their clinical use, 917
Softening about the right calcarine fissure associated with left hemianopsia, 552
Spiller, W. G., a report of two cases of multiple sclerosis, 61
Spinal cord, tubercular tumor of, 344
Stengel, A., articular rheumatism and some allied conditions, 412
Sterilization, artificial, 362
of phthisical women, 169
Stewart, D. D., gallstone disease, with special reference to diagnosis and treatment, 851
Stomach, carcinoma of, 557
Streptothrices, 373
Suppression of urine, total, in pregnant and non-pregnant animals, 544
Supravaginal amputation for fibroid, after-effects of, 364
Surgical intervention for intestinal perforation in a case of typhoid fever, 726
Sydenham's chorea, treatment of, 729
Synthetic salts of the nucleids of iron, copper, mercury, and silver, new series of, 350
Syphilis, hereditary, tabes in, 345
Syphilitic erythema nodosum, 934
Systolic mitral murmurs, 663

TABES in hereditary syphilitics, 345
Temporal bone, anatomy and surgery of, 563
Testicular ectopy, treatment of, 160
Tetanus antitoxin, preventive and curative action of, 935
Texas, malarial fever in, 448
Therapy, physical, 352
Thyroid extirpation in rabbits, pathological changes following, 746
gland, mixed tumors of, 243
tumor, removal of, at base of tongue, 926
Tonsil, fibrosarcoma of, 176
Torsion of the entire mesentery, 799
Tourniquet, treatment by, to counteract the vasomotor spasm of Raynaud's disease, 346
Toxicology of adrenalin, 727
Tropical abscess of liver, 210
Trunecek, serum of, in arterio-sclerosis, 351
Tubal gestation, 545

Tubercle bacilli, passage of, into the lymphatic and thoracic duct after ingestion, 554
Tubercular tumor of spinal cord, 344
Tuberculin, study of, 919
Tuberculosis, genital, 550
injections of yolk of egg for, 541
of appendix and adnexa, 170
of tongue, 927
pulmonary, treatment of, 916
Tuberculous dacryoadenitis and conjunctivitis, 183
meningitis, 731
with abnormal onset, 730
pleurisies, cytological study of, 558
Tubes, sounding of, 923
Turpentine in metrorrhagia, 364
Typhoid fever, abscesses of liver following, 618
acetozone in, 1106
bacillus of, viability of, 913
intestinal perforation during course of, 821
patients, presence of bacillus of Eberth in blood of, 938
serumtherapy of, 936
surgical intervention for intestinal perforation in the course of a case of, 726
treatment of, 167
Widal's test for the diagnosis of, 661

UNILATERAL renal hæmaturia, 636
Urea, pure, and pulmonary tuberculosis, 916
Ureteritis in the female, 284
Ureters, complete bilateral duplication of, 428
Urethra fibromyoma of, 171
Urethral caruncles, 925
Urobilinuria during pregnancy as a sign of fœtal death, 175
Uterine mucosa, atrophy of, 924
Uterus, abscess of, 171
and vagina, extirpation of, for procidentia, 924
cancer of, radical operation for, 740
treatment of, 362
complete inversion of, 360
dilatation of, by Bossi's dilator, 358
duplex separatus, 363
lymphosarcoma of, 923
perforation of, 169
rupture of, 172
Uterus, senile, structure of, 168
Uveal tract, sympathetic inflammation affecting the posterior part of, 183
Uvula, supernumerary, 177

VAGINAL examination, diagnosis of, 356
hysterectomy, 739
ovariotomy, 739
use of elastic bags, 174
Vaginofixation and ventrofixation, 738
Van Harlingen, A., epicarin in tinea tonsurans and tinea circinata, 1012
Vasomotor spasm of Raynaud's disease, 346
Vaughan, G. T., volvulus of the small intestine, 799
Veins, entrance of air into, 519
Vichy waters, alkaline, therapeutic value of, 351
Virus of variola, cultivation of, 372
Visual sensations, subjective, 1113
Volvulus of small intestine, 799
Vomiting, recurrent, in children, 629
Vulvovaginitis, gonorrheal, in children, 311

WAKEMAN, A. J., on adrenalin glycosuria and certain relations between the adrenal glands and carbohydrate metabolism, 46
Warbasse, J. P., peritonitis of the duodenal region, 882
Weil's disease, 158
Weir, W. H., eosinophilia in pelvic lesions and in the vermiform appendix, 74
Whitman, R., new method of correcting flexion deformity of knee-joint, 770
Widal reaction in Weil's disease, 158
Woldert, A., malarial fever in Texas, 448
Wolff, A. J., new method for the application of Widal's test for the diagnosis of typhoid fever, 661
Wood, A. C., case of gangrene of lung, 1060
Woods, R. F., gonorrhœal vulvovaginitis in children, 311
Woolley, P. G, adrenal tumors, 33
Wounds of the eye, treatment of, 367
Wright, J., notes from the throat department of the pathological laboratory of the Manhattan Eye and Ear Hospital, 1079

X-RAY, therapeutic efficacy of, 85
treatment in malignant diseases, 238
of carcinoma, 352

ZOMOTHERAPY in tuberculosis, 1071

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ORIGINAL ARTICLES.

AMYOTROPHIC LATERAL SCLEROSIS 939
BY JOSEPH COLLINS, M.D.

CONGENITAL DISLOCATION OF THE SHOULDER 967
BY CHARLES GREENE CUMSTON, M.D.

A CASE OF MYELOGENOUS LEUKÆMIA, WITH SEVERAL UNUSUAL FEATURES (ABSENCE OF EOSINOPHILIC LEUCOCYTES) 984
BY CHARLES E. SIMON, M.D.

THE DERMATOSES OCCURRING IN EXOPHTHALMIC GOITRE 1000
BY JAMES NEVINS HYDE, M.D., and ERNEST L. McEWEN, M.D.

NOTES ON THE EMPLOYMENT OF EPICARIN IN TINEA TONSURANS AND TINEA CIRCINATA 1013
BY ARTHUR VAN HARLINGEN, M.D., and HENRY K. DILLARD, JR., M.D.

THE BLOOD-PRESSURE REACTION OF ACUTE CEREBRAL COMPRESSION, ILLUSTRATED BY CASES OF INTRACRANIAL HEMORRHAGE 1017
BY HARVEY CUSHING, M.D.

A REVIEW OF SOME OF THE OLDER WRITINGS ON INFANT FEEDING 1044
BY SAMUEL McC. HAMILL, M.D.

A CASE OF GANGRENE OF THE LUNG CURED BY OPERATION 1060
BY DAVID RIESMAN, M.D., A. C. WOOD, M.D., and C. E. PFAHLER, M.D.

ZOMOTHERAPY IN TUBERCULOSIS 1071
BY LAWRASON BROWN, M.D.

NOTES FROM THE THROAT DEPARTMENT OF THE PATHOLOGICAL LABORATORY OF THE MANHATTAN EYE AND EAR HOSPITAL 1079
BY JONATHAN WRIGHT, M.D.

REVIEWS 1095

PROGRESS OF MEDICAL SCIENCE 1099

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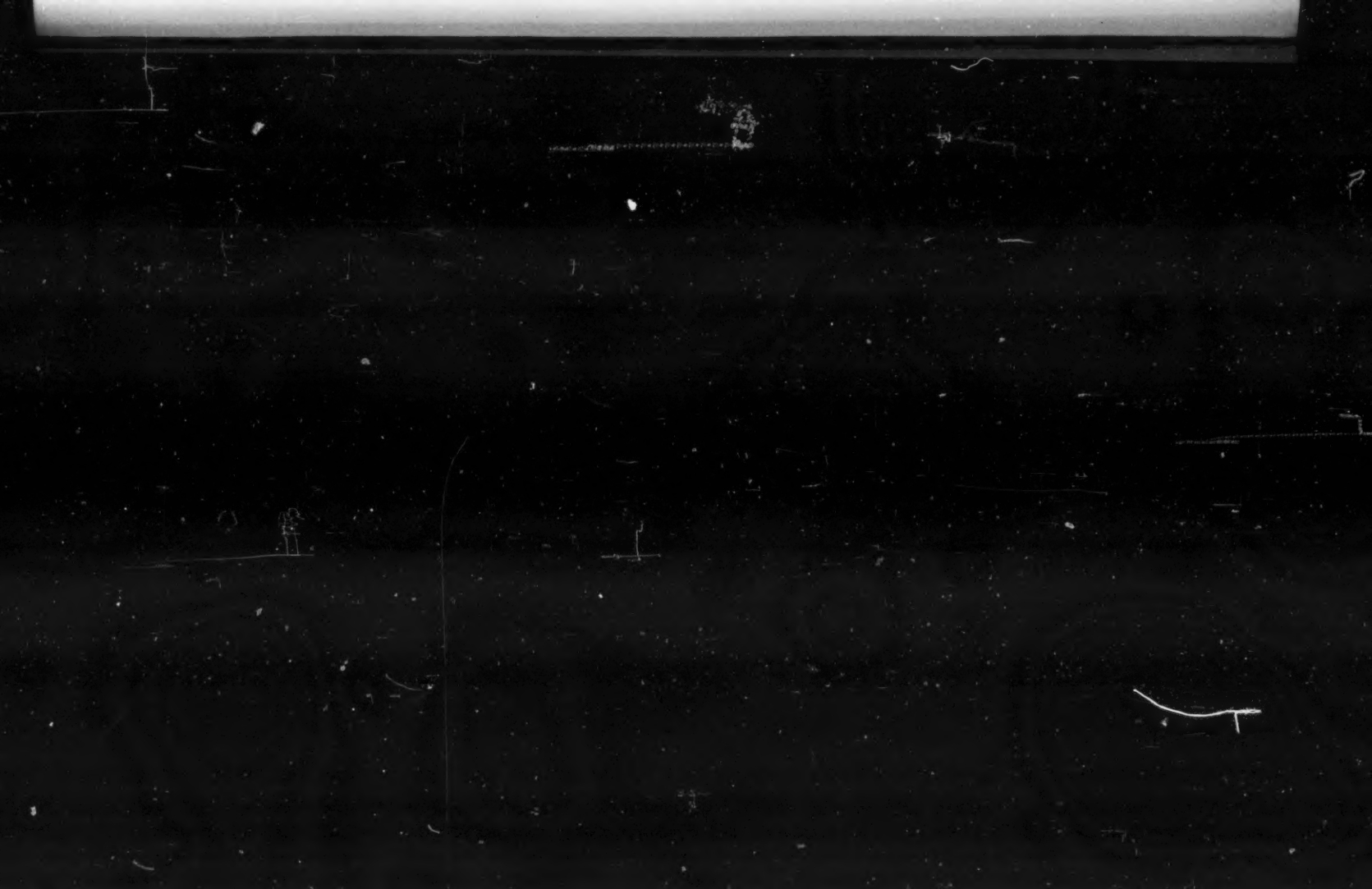

CONTENTS.

ORIGINAL COMMUNICATIONS.

PAGE

Sarcoma of the Third Cervical Segment: Operation; Removal; Continued Improvement. By JAMES W. PUTNAM, M.D., WILLIAM C. KRAUSS, M.D., and ROSWELL PARK, A.M., M.D., LL.D. . 1

Studies of Ovarian Embryomata, or So-called Ovarian Dermoid Cysts. By WILLIAM FREDERICK JELKE, M.D. 6

Adrenal Tumors. By PAUL G. WOOLLEY, B.S., M.D. . . . 33

On Adrenalin Glycosuria and Certain Relations between the Adrenal Glands and Carbohydrate Metabolism. By C. A. HERTER, M.D., and A. J. WAKEMAN, PH.D. 46

A Report of Two Cases of Multiple Sclerosis, with Necropsy: with Remarks on Muscular Atrophy, Secondary Degeneration, and Loss of Tendon Reflexes, with Increased Muscular Tonicity, Occurring in this Disease. By WILLIAM G. SPILLER, M.D. . 61

Eosinophilia in Pelvic Lesions and in the Vermiform Appendix. By WILLIAM H. WEIR, M.D. 74

The Pathology of the Tissue Changes Induced by the X-ray: Preliminary Report. By A. G. ELLIS, B.S., M.D. 85

Paracolon Infections, with Report of Three Cases. By HERBERT W. ALLEN, M.D. 96

Malta Fever: Its Occurrence in the United States Army, with a Review of the Literature. By CHARLES F. CRAIG, M.D. 105

On Multiple Serositis—the Association of Chronic Obliterative Pericarditis with Ascites, with Particular Reference to the "Pericarditic Pseudocirrhosis of the Liver" of Pick and the "Iced Liver" (Zuckergussleber) of Curschmann. By ALOYSIUS O. J. KELLY, A.M., M.D. 116

REVIEWS.

American Edition of Nothnagel's Encyclopædia of Practical Medicine. Typhoid Fever and Typhus Fever. By Dr. H. Curschmann . . 149

The Principles and Practice of Gynecology, for Students and Practitioners. By E. C. Dudley, A.M., M.D. 150

Bericht ueber die von Komitee für Krebsforschung am 15 Oktober, 1900, erhobene Samelforschung. Report on the Collective Investigation Made by the Committee for the Investigation of Cancer. Edited by the Directors, Professors von Leyden, Kirchner, von Hansemann and Meyer, and Dr. Wutzdorff 152

American Edition of Nothnagel's Encyclopædia. By William P. Northrup, M.D. 153

Reynolds and Newell's Practical Midwifery. By Edward Reynolds, M.D., and Franklin S. Newell, M.D. 154

A Text-Book of Diseases of the Ear for Students and Practitioners. By Professor Dr. Adam Politzer, of Vienna 155

The Physician's Visiting List for 1903 156

The Medical News Visiting List for 1903 156

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

	PAGE		PAGE
Œdema of the Lower Limbs. .	157	The Presence of the Widal Reaction in Weil's Disease . .	158
Acute Polymyositis . . .	158		

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

AND

F. D. PATTERSON, M.D.

	PAGE		PAGE
The Treatment of Testicular Ectopy	160	Operation for Paralytic Club-foot .	162
Resection of Nearly Eight Feet of Gangrenous Intestine; Recovery	161	The Use of Argyrol in the Treatment of Acute Gonorrhœa . .	163

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

	PAGE		PAGE
Antagonism of Morphine and Cocaine and the Employment of Cocaine in Morphine-poisoning	164	The Diphtheria Serum Question .	166
Camphor and the Morphine Disease	165	A Case of Poisoning from Pennyroyal.	166
A Fake Morphine Cure . .	165	Treatment of Typhoid Fever .	167
Arsenic in the Treatment of Phthisis	166	Impermeability of the Lung for Ammonia	167
		Affinity of Carbonic Oxide for Hæmoglobin	167

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

	PAGE		PAGE
Laparotomy for Adherent Retroflexion during Pregnancy	168	Perforation of the Uterus	169
Lymphangiectasis of the Vulva	168	Tuberculosis of the Appendix and Adnexa	170
Premature Menopause	168	The Malignancy of Solid Embryomata	170
Structure of the Senile Uterus	168	Abscess of the Uterus	171
Sterilization of Phthisical Women	169	Menopause	171
Intra-abdominal Pressure	169	Artificial Distention of the Bladder	171
The Paravaginal Incision in Hysterectomy	169	Fibromyoma of the Urethra	171

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

	PAGE		PAGE
Pubiotomy	172	Urobilinuria during Pregnancy as a Sign of Fœtal Death	175
Rupture of the Uterus Through Cicatricial Tissue	172	The Estimation of the Transverse Diameter of the Pelvis in the Parturient Woman	175
Vaginal Use of Elastic Bags	174		
Quintuplets	175		

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.

	PAGE		PAGE
Rapid Development of a Fibrosarcoma of the Tonsil	176	Supernumerary Uvula	177
Œdematous Laryngitis	176	Fatal Membranous Glossitis	177
Adenoma of the Nose, with Incipient Sarcomatous Metamorphosis: Removal by External Access	176	A Durham Tube in the Right Bronchus	177
Phlegmonous Laryngitis	177	The Chemical Pathology of the Saliva and of the Pharyngeal Secretions as a Means of Diagnosis	178

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

AND

MILTON B. HARTZELL, M.D.

	PAGE		PAGE
The Occurrence of Bullæ in Lichen Planus	178	Psoriasis following Nervous Shock	179
A Case of Hyphomycetic Granuloma of the Skin	178	The Treatment of Lupus Vulgaris by Applications of Radium	180
Primary Actinomycosis of the Occiput	179	Psoriasis following Vaccination	180
A Case of Dermatitis Verrucosa Probably Caused by Bacillus Coli Communis	179	Noma and Hospital Gangrene	180
		An Anomalous Superficial Dermatitis Occurring during Typhoid Fever and Having Some Resemblance to Psoriasis Rupioides	181

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.

	PAGE		PAGE
Etiology of Myopia	181	Treatment of Incipient Cataract by Collyria and Ocular Baths of Iodine	183
A Study of the Sense of Sight Shortly after Operations Successfully Performed on Adults for Congenital Blindness	182	Treatment of Diphtheritic Conjunctivitis by the Instillation of Antitoxin into the Conjunctival Sac	183
The Nerve Supply of the Lacrymal Gland	182	Tuberculous Dacryoadenitis and Conjunctivitis	183
Inflammation Affecting Posterior Part of Uveal Tract	183		

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.

AND

EDWARD F. WILLOUGHBY, M.D.

	PAGE
Causation of Beriberi	184
The Presence and Vitality of Bacteria in Oils	186

CONTENTS.

ORIGINAL COMMUNICATIONS.

PAGE

Diseases of the Pancreas. By JOHN B. DEAVER, M.D. . . . 187
Tropical Abscess of the Liver, with Report of a Case. By SOLOMON SOLIS COHEN, M.D., and JOHN H. GIBBON, M.D. . . . 210
A Study of Some Cirrhoses of the Liver. By BEVERLEY ROBINSON, M.D. 215
A Case of Multiple Melanotic Sarcoma Unsuccessfully Treated by X-rays. By JAMES P. MARSH, M.D. 238
Mixed Tumors of the Thyroid Gland. By LEO LOEB, M.D. . . 243
The Pathology of Labial and Nasal Herpes and of Herpes of the Body Occurring in Acute Croupous Pneumonia, and Their Relation to the So-called Herpes Zoster. By WM. TRAVIS HOWARD, JR., M.D. 256
An Experimental Study of Lithium. By CLARENCE A. GOOD, M.D. . 273
Ureteritis in the Female. By EDGAR GARCEAU, M.D. . . . 284
Gonorrhœal Vulvovaginitis in Children. By RICHARD F. WOODS, A.M., M.D. 311
Memoir of J. M. Da Costa, M.D. By MARY A. CLARKE . . . 318

REVIEWS.

A Treatise on Diseases of the Skin. By Henry W. Stelwagon, M.D., Ph.D. 330
A Manual of Surgical Treatment. By Watson Cheyne, M.B., F.R.C.S., F.R.S., and F. F. Burghard, M.D., M.S., F.R.C.S. . . . 332
A Treatise on the Diseases of the Throat and Nose and Associated Affections of the Ear. By Charles P. Grayson, M.D. . . . 334
A Treatise on Massage: Its History, Mode of Application, and Effects. By Douglas Graham, M.D. 335
Taschenbuch der Massage für Studirende und Aerzte. Von Dr. Erich Ekgren 335
A Pocketbook on Massage 335
Morphinism and Narcomania from Opium, Cocaine, Ether, Chloral, Chloroform, and Other Narcotic Drugs. By T. D. Crothers, M.D. 336
A Practical Treatise on Smallpox. By George Henry Fox, A.M., M.D. 337
The Healing of Nerves. By Charles A. Ballance, M.S., F.R.C.S., and Purvis Stewart, M.A., M.D., M.R.C.P. 337
An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations. By George W. Crile, A.M., M.D., Ph.D. 338
A System of Physiologic Therapeutics. Edited by Solomon Solis Cohen, A.M., M.D. 339

PAGE
Chirurgie Gastro intestinale. By Henri Hartmann, M.D. . . . 340
Charaka-Samhita (translated into English) 340
A Text-Book of Practical Diagnosis. By Hobart Amory Hare, M.D. 340
International Clinics. Edited by Henry W. Cattell, A.M., M.D. . 341
Traité de Chirurgie Clinique et Operatoire 341
Water and Water Supplies. By John C. Thresh, D.Sc. (London), M.D. (Victoria), D.P.H. (Cambridge) 342
Original Researches in the Treatment of Tropical Diseases with Indigenous Drugs, etc. By Hem Chandra Sen, M.D. (Cal.) . . 343
A Thesis on Tropical Abscess of the Liver. By Hem Chandra Sen, M.D. (Cal.) 342

PROGRESS OF MEDICAL SCIENCE

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

PAGE
The Early Diagnosis of Attacks and Relapses of Acute Articular Rheumatism 343
Case of Tubercular Tumor of the Spinal Cord in a Child Two Years Old 344
On a Powerful Specific for the Treatment of Malarial Fever . 345
Tabes in Hereditary Syphilitics . 345
Treatment by the Tourniquet to Counteract the Vasomotor Spasm of Raynaud's Disease . . 346

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

AND

F. D. PATTERSON, M.D.

PAGE
The External Dorsal Luxation of the Metacarpophalangeal Joint of the Thumb 347
Femoral Osteotomy and Ostectomy in Ankylosis of the Hip . . 348
The Fracture of Dupuytren . . 349

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

	PAGE
Concerning a New Series of Synthetic Salts of the Nucleids of Iron, Copper, Mercury, and Silver	350
Peridynamin	351
The Serum of Trunecek in Arteriosclerosis	351
Agurin: A New Diuretic	351
The Therapeutic Value of the Alkaline Vichy Waters	351
Physical Therapy	352
Dangers of Subcutaneous Gelatin Injections	352
X-ray Treatment of Carcinoma	352
Drops as Dose Measures	352
Relation Between the Chemistry and the Physiological Action of Morphine	353
Decomposition of Iodides in the Body	354
Some Principles of the Brain of the Horse	354

PEDIATRICS.

UNDER THE CHARGE OF

LOUIS STARR, M.D.,

AND

THOMPSON S. WESTCOTT, M.D.

	PAGE
The Leucocyte Count in the Diagnosis of Diseases of Children	355

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

	PAGE
Diagnosis by Vaginal Examination	357
Rapid Dilatation of the Uterus by Bossi's Dilator	358
Complete Inversion of the Uterus of Seven Months' Duration	360
Treatment of Face Presentation with Posterior Turning of Chin	360

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

	PAGE		PAGE
Artificial Sterilization	362	Turpentine in Metrorrhagia	364
Influence of Gonococcus in Pregnancy and the Puerperium	362	After-effects of Supravaginal Amputation for Fibroid	364
Treatment of Cancer of the Uterus	362	Ovarian Tumors Complicating Pregnancy	365
Herpes of the Larynx during Menstruation	363	Retroperitoneal Lipoma and Uterine Fibroid	365
Uterus Duplex Separatus	363	Ethyl Chloride in the Treatment of Incurable Cancer	365
Malignant Folliculoma of Ovary	363	Ligation of Internal Iliac and Ovarian Arteries in Cancer of Uterus	365
Pulmonary Embolism following Hysterectomy	364		
Parotitis after Ovariotomy	364		

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.

	PAGE		PAGE
Etiology of Myopia	366	The Cortical Centres of Vision as Demonstrated after Enucleation or Atrophy of the Eyeball	368
Course of Fibres in Optic Nerve as Shown by Their Degeneration	366	Treatment of Ophthalmia Neonatorum	368
Immediate Treatment of Wounds of the Eye	367		

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

AND

F. P. GAY, M.D.

	PAGE		PAGE
The Pathological Changes in Hodgkin's Disease	370	The Pathology of Lymphotoxic and Myelotoxic Intoxication	373
Diphtheria Bacillus in Well Persons	372	Actinomyces-like Development of Acid-resisting Bacilli	373
Cultivation of the Virus of Variola	372	Bacteriological Findings in an Epidemic of Dysentery in Syria	374
The Sensibilizers of Sera Active against Albuminoid Substances	373		

CONTENTS.

ORIGINAL COMMUNICATIONS.

PAGE

Metastatic Carcinoma of the Choroid. With Report of a Case and Review of the Literature. By E. L. OATMAN, M.D. . . . 375

A Report of Cases of Anæmia, with Observations upon Their Symptoms and Morphology of the Blood. By J. ALISON SCOTT, M.D. 397

A Case of Banti's Disease, with Diffuse Productive Nephritis. By CYRUS W. FIELD, M.D. 405

Articular Rheumatism and Some Allied Conditions. By ALFRED STENGEL, M.D. 412

Two Cases of Complete Bilateral Duplication of the Ureters. By A. H. GOULD, M.D. 428

Aphasia in Acute Disease, with Report of a Case Complicating Smallpox. By CHARLES J. ALDRICH, M.D. 431

The Clinical Value of Blood Pressure Determinations as a Guide to Stimulation in Sick Children. By HENRY WIREMAN COOK, M.D. 433

Malarial Fever in Texas: The Financial Loss Arising from the Disease, and Its Prevention. By ALBERT WOLDERT, M.D. . . . 448

Upon the Association of Epilepsy and Heart Disease. By T. L. CHADBOURNE, M.D. 461

Hydatiform Mole: With a Report of Two Cases and Clinical Deductions from Two Hundred and Ten Reported Cases. By PALMER FINDLEY, M.D. 486

Entrance of Air into the Veins. A Reply to Dr. Hare. By MALCOLM GOODRIDGE, M.D. 519

REVIEWS.

A Treatise on Diseases of the Eye, Ear, Nose, and Throat. Edited by William Campbell Posey, A.B., M.D., and Jonathan Wright, M.D. 524

Diseases of the Eye. A Handbook of Ophthalmic Practice for Students and Practitioners. By G. E. de Schweinitz, A.M., M.D. . . 525

Dilatation of the Stomach. By M. Soupault. 527

A Handbook of Materia Medica, Pharmacy, and Therapeutics. By Samuel O. L. Potter, A.M., M.D., M.R.C.P. 527

The Diseases of Infancy and Childhood. By Henry Koplik, M.D. . 528

PAGE

Biological Laboratory Methods. By P. H. Mell, Ph.D. 529
The Public and the Doctor. By a Regular Physician 530
A Reference Handbook of the Medical Sciences, Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. Edited by Albert H. Buck, M.D. 530
The Practical Medicine Series of Year Books, Comprising Ten Volumes on the Year's Progress in Medicine and Surgery. Edited by Frank Billings, M.S., M.D., and J. H. Salisbury, M.D. 530

PROGRESS OF MEDICAL SCIENCE

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

PAGE

Incidence of Alkaptonuria: A Study in Chemical Individuality . 531
Diabetes Insipidus, with a Report of Five Cases 532
Scarlatiniform Erythema in Tuberculosis 533
Cutaneous Angiomata in the Diagnosis of Malignant Disease . 534

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

AND

F. D. PATTERSON, M.D.

PAGE

The Anastomosis of the Portal Vein with the Vena Cava . . . 535
Growth of Bacteria in the Intestine 535
Intracapsular Prostatic Resection. The Normal Method in Cases of Prostatic Hypertrophy . . 537
Two Cases of Obscure Abdominal Pain; Operations; Results . 538
Treatment of Cancerous Affections of the Skin by Means of X-rays . 539
The Treatment of Fractures of the Extremities 540

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

	PAGE		PAGE
Treatment of Pneumonia	540	Pseudoaconitine and Japaconitine	542
Action of Heroin and Dionin on Respiration	541	Mannitol Pentanitrate	542
Injections of Yolk of Egg for Tuberculosis	541	Treatment of Graves' Disease	542
		Hypodermic Purgatives	543
		Phenolphthalein as a Purgative	543

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

	PAGE		PAGE
The Result of Total Suppression of Urine in Pregnant and Non-pregnant Animals	544	Duration of Lactation	546
Tubal Gestation	545	The Production of Eclampsia	547
		Cæsarean Section for Placenta Prævia	548

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

	PAGE		PAGE
Hot Air in Gynecological Treatment	548	Diagnosis of Genital Tuberculosis	550
Fibromyoma Complicated with Pregnancy	548	The Treatment of Pelvic Suppuration	550
Laparotomy during Pregnancy	549	Treatment of Retroflexion	551
Anatomy of Chronic Parametritis	550	Diabetes in Gynecological Operations	551

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.

	PAGE		PAGE
Ablation of the Crystalline Lens to Rectify High Myopia	551	Softening about the Right Calcarine Fissure Associated with Left Hemianopsia	552
Optic Neuritis in Diphtheria	551	Treatment of Phlyctenular Keratitis	552
When to Operate for Senile Cataract, the Other Eye Possessing Useful Vision	552	Restoration of Sight in a Nearly Blind Cancerous Eye by Cancroin	553

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

AND

F. P. GAY, M.D.

	PAGE		PAGE
Cyst of the Pancreas	553	A House Epidemic of a Fever Simulating Typhoid, Caused by an Atypical Colon Bacillus	556
The Passage of Tubercle Bacilli into the Lymphatic and Thoracic Duct after Ingestion	554	The Question of Fat Absorption in the Intestinal Canal and the Transport of Fat to Other Organs	556
Experimental Investigations upon the New Formation of Inflammatory Granulation Tissue	554	The Presence of Elastic Tissue in Carcinoma of the Stomach	557
Gonorrhœal Endocarditis with Cultivation of the Specific Organism from Blood during Life	555	Contribution to the Cytological Study of Tuberculous Pleurisies	558

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.

AND

EDWARD F. WILLOUGHBY, M.D.

	PAGE
The Cause of Beriberi	558
Distribution of Sewage Bacteria in Drinking Water	560
Infection through Droplets and Dust	561

CONTENTS.

ORIGINAL COMMUNICATIONS.

PAGE

A Contribution to the Anatomy and Surgery of the Temporal Bone. By A. E. SCHMITT, M.D. 563

Gangrenous Cholecystitis, with a Report of a Case in Which a Successful Cholecystectomy was Done. By JOHN H. GIBBON, M.D. . 592

Jaundice, with Reports of Interesting Illustrative Cases—a Contribution to the Toxic Forms of this Condition. By JAMES M. ANDERS, M.D., LL.D. 596

Abscesses of the Liver following Typhoid Fever. By JOHN G. SHELDON, M.D. 618

A Preliminary Communication Concerning the Nature and Treatment of Recurrent Vomiting in Children. By DAVID L. EDSALL, M.D. 629

Unilateral Renal Hæmaturia. By AUGUSTUS A. ESHNER, M.D. . 636

Bence Jones Albumosuria, with Peculiar Nervous Phenomena. By L. NAPOLEON BOSTON, A.M., M.D. 658

On a New Method for the Application of Widal's Test for the Diagnosis of Typhoid Fever. By ARTHUR J. WOLFF, M.D. . . 661

Late Systolic Mitral Murmurs. By J. N. HALL, M.D. . . . 663

Concerning the Role of Intracellular Catalytic Processes in the Pathogenesis of Malignant Neoplasms. By JOHN C. HEMMETER, M.D., Ph.D. 666

Rubber Tissue as a Dressing. By G. TUCKER SMITH, M.D. . . 704

REVIEWS.

Handbook of Pathogenic Micro-organisms. Edited by Profs. W. Kolle and A. Wassermann 706

The International Text-book of Surgery, by American and British Authors. Edited by J. Collins Warren, M.D., LL.D., Hon. F.R.C.S. Eng., and A. Pearce Gould, M.S., F.R.C.S. 707

General Paresis, Practical and Clinical. By Robert Howland Chase, A.M., M.D. 708

Diseases of the Stomach: Their Pathology, Diagnosis, and Treatment, with Sections on Anatomy, Physiology, Chemical and Microscopic Examination of Stomach Contents, Dietetics, Surgery of the Stomach, etc. By John C. Hemmeter, M.D, Ph.D. 709

Studies of the Internal Anatomy of the Face. By M. H. Cryer, M.D. 711

Clinical Psychiatry. A Text-book for Students and Physicians. By A. Ross Defendorf, M.D. 712

Medical Microscopy: Designed for Students in Laboratory Work and for Practitioners. By T. E. Oertel, M.D. 712

PAGE

A Manual of Genito-urinary and Venereal Diseases. For the Use of Students and Practitioners. By Louis E. Schmidt, M.D. . . 712
The American Year Book of Medicine and Surgery for 1903. Edited by George M. Gould, A.M., M.D. 713
Progressive Medicine. Edited by Hobart Amory Hare, M.D. . . 713
Clinical Methods: A Guide to the Practical Study of Medicine. By Robert Hutchison and Harry Rainy 714
Les Difformités Acquises de l'Appareil Locomoteur Pendant l'Enfance et de l'Adolescence. Par le Dr. Kirmisson 715
Lectures on Chemical Pathology in its Relation to Practical Medicine. By C. A. Herter, M.D. 715
A Text-book of Materia Medica, Therapeutics, and Pharmacology. By George F. Butler, Ph.G., M.D. 716
Physical Diagnosis: Diseases of the Thoracic and Abdominal Organs. By Egbert Le Fevre, M.D. 717
Saunders' Question Compends, No. 25. Essentials of Histology. By Louis Leroy, B.S., M.D. 717
A Text-book of Anatomy, by American Authors. Edited by Frederic Henry Gerrish, M.D. 718

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

PAGE

An Epidemic of Paratyphoid Fever 719
Acute Infectious Diseases . . . 720
The Nature of Non-tropical Chyluria 721

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

AND

F. D. PATTERSON, M.D.

PAGE

An Operation for the Radical Cure of Aneurism Based upon Arteriorrhaphy 723
Remarks on a Second Series of Fifty Cases of Recurrent Appendicitis Treated by Operation . 725
Chloride of Ethyl in Anæsthesia . 726
Surgical Intervention for Intestinal Perforation in the Course of a Case of Typhoid Fever; Recovery 726
Note on the Value of Roux's Operation for the Radical Cure of Femoral Hernia 727

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

	PAGE		PAGE
Toxicology of Adrenalin . .	727	Treatment of Sydenham's Chorea by Arsenic	729
Anæsthesin	729	Guaiacol Valerianate in Phthisis .	730
The Active Principles of Rhubarb	729		

PEDIATRICS.

UNDER THE CHARGE OF

LOUIS STARR, M.D.,

AND

THOMPSON S. WESTCOTT, M.D.

	PAGE		PAGE
Tuberculous Meningitis, with Abnormal Onset	730	Rubella Scarlatinosa . . .	731
A Case of Cured Tuberculous Meningitis	731	Empyema in Children . . .	732
		Infantile Scorbutus and Sterilized Milk	733

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

	PAGE		PAGE
The Efficiency of Disinfection of the Hands by Hot Water and Alcohol	735	Most Efficient Preparation of Ergot	736
Two Cases of Pregnancy and Labor Complicated by Atresia and Stenosis of the Vagina . .	735	Cæsarean Section by Transverse Incision of the Fundus . .	736
		Hydatiform Mole, with the Report of 2 Cases and Collection of 210 Cases	737

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

	PAGE		PAGE
Adenoma Malignum . . .	738	Vaginal Hysterectomy . . .	739
Vaginofixation and Ventrofixation	738	Vaginal Ovariotomy . . .	739
Benign Epithelial Proliferation in the Corpus Uteri . . .	738	Ovarian Parotitis	740
Leucocytosis in Pelvic Suppuration	739	Radical Operation for Cancer of the Uterus	740
Alcohol as a Disinfectant . .	739	Cancer of the Uterus . . .	740

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.

	PAGE		PAGE
Sarcoma of Branchial Cleft	741	Nasal Polypi the Cause of Atrophy of the Optic Nerves	742
True Papilloma of the Nasal Septum	741	Foreign Body in the Larynx	742
Morbid Growths of the Nose: Osteosarcoma of the Inferior Turbinate	741	Morbid Growths of the Larynx	742
Angiofibroma of the Nose	742	Foreign Bodies in the Air Passages: Escape of the Outer Tube of a Durham Tracheal Canula	743

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

AND

F. P. GAY, M.D.

	PAGE		PAGE
Multiple Progressive Hyalosero-sitis	743	the Formation of Agglutinins in the Bodies of Embryos	745
The Intestinal Origin of the So-called "Fever of Infancy" (Fiebre de Borras)	745	A Contribution to the Knowledge of the Pathological Changes following Thyroid Extirpation in Rabbits	746
The Inheritance and Intra-uterine Transmission of the Agglutinating Properties of the Blood and		Relations Between the Lymphatics and the Connective Tissue	746

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.

AND

EDWARD F. WILLOUGHBY, M.D.

	PAGE
Ptomaine Poisoning	747
Scurvy: a Chronic Ptomaine Poisoning	749

CONTENTS.

ORIGINAL COMMUNICATIONS.

PAGE

Anatomical Study of a Short-limbed Dwarf, with Special Reference to Osteogenesis Imperfecta and Chondrodystrophia Fœtalis. By LUDVIG HEKTOEN, M.D. 751

A New Method of Correcting Flexion Deformity at the Knee-joint. By ROYAL WHITMAN, M.D. 770

Pronation of the Foot. By E. J. HUHNER, M.D. 775

A Case of Aneurism of the Transverse Portion of the Aortic Arch in a Girl of Nine Years, with Table of Reported Cases under Twenty Years of Age. By THEODORE LE BOUTILLIER, M.D. 778

Some Notes on the Opium Habit and Its Treatment. By SMITH ELY JELLIFFE, M.D., Ph.D. 786

Volvulus of the Small Intestine—Its Relations to Hernia. Torsion of the Entire Mesentery. Report and Résumé of Cases. By GEORGE TULLY VAUGHAN, M.D. 799

Intestinal Perforation during the Course of Typhoid Fever, and Its Surgical Aspects. By C. E. BRIGGS, M.D. 821

Some Phases of Gallstone Disease, with Special Reference to Diagnosis and Treatment. By D. D. STEWART, M.D. 851

Peritonitis of the Duodenal Region. By JAMES P. WARBASSE, M.D. . 882

A Contribution to the Study of the Human Blood Pressure in Some Pathological Conditions. By GEORGE WM. NORRIS, A.B., M.D. . 888

REVIEWS.

Materia Medica, Therapeutics, Medical Pharmacy, Prescription-writing, and Medical Latin. By William Schleif, Ph.G., M.D. . 903

A Compend of Human Physiology. By Albert P. Brubaker, M.D. . 904

A Text-book of Surgical Principles and Surgical Diseases of the Face, Mouth, and Jaws, for Dental Students. By H. Horace Grant, A.M., M.D. 904

A Manual of Medical Treatment or Clinical Therapeutics. By J. Burney Yeo, M.D. 905

A Text-book of Pathology and Pathological Anatomy. By Dr. Hans Schmaus. 905

A Manual of Materia Medica and Pharmacology. By David M. R. Culbreth, Ph.G., M.D. 906

PAGE

Atlas and Epitome of Diseases of the Mouth, Pharynx, and Nose. By Dr. L. Grunwald. 907
Anatomy and Histology of the Mouth and Teeth. By I. N. Brownell, M.D. 907
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PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

PAGE

Acute Nephritis following Mumps . 911
On the Working Capacity of the Heart 911
Effects of Freezing and Other Low Temperatures upon the Viability of the Bacillus of Typhoid Fever 913

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

PAGE

A New System of Treating Pulmonary Phthisis . . . 916
Methylene Blue and Quinine in Malaria 916
Urea and Pulmonary Tuberculosis . 916
Sodium and Potassium Iodides and Their Clinical Use . . . 917
Morphine Addiction and Its Treatment 917
Two New Drugs: Hopogan and Extogan 918
A Study of Tuberculin 919
Hyoscine for the Morphine Disease 919

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

	PAGE		PAGE
Hydatid Mole	920	Intraperitoneal Hemorrhage and Ectopic Gestation . . .	921
Fœtal and Maternal Blood Serum .	920		

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

	PAGE		PAGE
Surgical Treatment of Parametric Cicatrices	922	Profuse Hemorrhage from a Ruptured Ovisac	923
Results of Myomectomy and Castration	922	Extirpation of the Uterus and Vagina for Procidentia . .	924
The Relation of Dyspepsia to Pelvic Disease	923	Pruritus Vulvæ	924
Sounding of the Tubes . . .	923	Urethral Caruncles . . .	924
Lymphosarcoma of the Uterus .	923	Atrophy of the Uterine Mucosa .	925
		Primary Cancer of Fallopian Tube	925

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.

	PAGE		PAGE
Saddle-back Nose	926	Primary Tuberculosis of Tongue	927
Primary Nasal Diphtheria . .	926	Foreign Bodies (Coins) in the Œsophagus of Infants . .	927
Parotiditis	926	Falsetto Voice	928
Removal of an Accessory Thyroid Tumor at the Base of the Tongue	926	Sarcoma of the Maxillary Sinus .	928
		Lupus of the Epiglottis . .	928

OTOLOGY.

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

ASSISTED BY

E. A. CROCKETT, M.D., P. HAMMOND, M.D., E. DE WOLF WALES, M.D.,

AND

WALTER A. LECOMPTE, M.D.

	PAGE		PAGE
Contribution to the Bacteriology of Otitis of Measles . . .	929	Neuroses and Mastoid Operations	930

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

AND

MILTON B. HARTZELL, M.D.

	PAGE		PAGE
A Case of Favus of the Scrotum Coexisting with Ringworm of the Thigh, Giving Identical Trichophyton-like Cultures . . .	931	Mycosis Fungoides and Its Treatment by the X-rays . . .	933
Dermatitis Coccidioides . .	931	Acute Symmetrical Erythematous Keratodermia Caused by the Administration of Arsenic . .	933
Treatment of Lupus Erythematosus	932	Erythema Scarlatiniforme Desquamativum Recidivans . . .	934
Alopecia Areata of the Moustache of Dental Origin . . .	932	Syphilitic Erythema Nodosum .	934

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

AND

F. P. GAY, M.D.

	PAGE		PAGE
On Changes in the Bacteriolytic Power of Blood after Typhoid Vaccination	935	Serumtherapy of Typhoid Fever .	936
Influence of Mode of Introduction on the Preventive and Curative Action of Tetanus Antitoxin .	935	Study of an Hæmolytic Complement Found in Serum of the Rabbit .	936
Preliminary Report of Appearance in Philippine Islands of a Disease Clinically Resembling Glanders	935	The Relationship Between Human and Bovine Tuberculosis . .	937
		Agglutination in Mixed Infections, and Their Means of Diagnosis .	937
		Presence of Bacillus of Eberth in Blood of Typhoid Fever Patients	938

CONTENTS.

ORIGINAL COMMUNICATIONS.

	PAGE
Amyotrophic Lateral Sclerosis. By JOSEPH COLLINS, M.D.	939
Congenital Dislocation of the Shoulder. By CHARLES GREENE CUMSTON, M.D.	967
A Case of Myelogenous Leukæmia, with Several Unusual Features (Absence of Eosinophilic Leucocytes). By CHARLES F. SIMON, M.D.	984
The Dermatoses Occurring in Exophthalmic Goitre. By JAMES NEVINS HYDE, M.D., and ERNEST L. MCEWEN, M.D.	1000
Notes on the Employment of Epicarin in Tinea Tonsurans and Tinea Circinata. By ARTHUR VAN HARLINGEN, M.D., and HENRY K. DILLARD, JR., M.D.	1012
The Blood-pressure Reaction of Acute Cerebral Compression, Illustrated by Cases of Intracranial Hemorrhage. A Sequel to the Mütter Lecture for 1901. By HARVEY CUSHING, M.D.	1017
A Review of Some of the Older Writings on Infant Feeding. By SAMUEL MCC. HAMILL, M.D.	1044
A Case of Gangrene of the Lung Cured by Operation. By DAVID RIESMAN, M.D., A. C. WOOD, M.D., and G. E. PFAHLER, M.D.	1060
Zomotherapy in Tuberculosis. By LAWRASON BROWN, M.D.	1071
Notes from the Throat Department of the Pathological Laboratory of the Manhattan Eye and Ear Hospital. By JONATHAN WRIGHT, M.D.	1079

REVIEWS.

Applied Surgical Anatomy Regionally Presented, for the Use of Students and Practitioners of Medicine. By George Woolsey, A.B., M.D.	1095
A Guide to the Practical Examination of Urine, for the Use of Physicians and Students. By James Tyson, M.D.	1097
The Elements of Bacteriological Technique: A Laboratory Guide for the Medical, Dental, and Technical Student. By J. W. H. Eyre, M.D., F.R.S. Edin.	1097
Anleitung zur Diagnose und Therapie der Kehlkoph-, Nasen-, und Ohrenkrankheiten. Von Dr. Richard Kayser	1098
The Mattison Method in Morphinism. By T. B. Mattison, M.D.	1098

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

AND

W. S. THAYER, M.D.

	PAGE
Metabolism in Albuminuria	1099
On the Micrococcus of Acute Rheumatism	1100

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

AND

F. D. PATTERSON, M.D.

On Four Cases of Perforating Gastric Ulcer, of which Three Recovered	1101
Operations for Gastric Ulcer, Acute and Chronic	1102
A Clinical Lecture on Some Cases Simulating Acute Appendicitis	1102
Hydatid Costal Cysts	1103
A Simple Method of Operating on Piles	1104

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

AND

SMITH ELY JELLIFFE, M.D., PH.D.

Intravascular Antisepsis	1105
The Treatment of Typhoid Fever by Acetozone	1106
Disodic Methyl-arsenate	1106

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

PAGE

Bossi's Dilator and Eclampsia 1108
Hyperpyrexia with Thrombosis of the Inferior Vena Cava . . . 1108
Laceration of the Vagina during Labor 1109
Double Pregnancy in Double Uterus 1110
Fœtal Ascites 1110

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Progressive Peritonitis 1111
Phenomena following Removal of the Adnexa 1112
Adenoma Malignum in a Young Woman 1112
Results of Alexander's Operation 1112
Venous Stasis as a Cause of Retro-uterine Hæmatocele 1112

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.

Subjective Visual Sensations 1113
The Cosmetic Value of Paraffin Injections after Enucleation of the Eyeball 1114

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

AND

F. P. GAY, M.D.

PAGE

Symposium on Snake Venom 1115
The Pancreas in Cirrhosis of the Liver 1116
Ring Bodies (Nuclear Remnants) in Anæmic Blood 1116

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.

AND

EDWARD F. WILLOUGHBY, M.D.

Action of Water on Lead 1117
Disinfection by Dry Heat 1118
The Neutral-red Method in the Differentiation of B. Coli and B. Typhosus 1118

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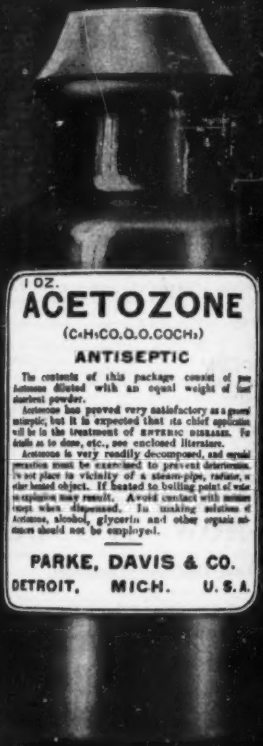
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